



CONTACT: Lisa Rossi
+1- 412- 916-3315 (mobile)
rossil@upmc.edu

FOR IMMEDIATE RELEASE

Microbicide Trials Network Statement on Decision to Discontinue Use of Oral Tenofovir Tablets in VOICE, a Major HIV Prevention Study in Women

PITTSBURGH, September 28, 2011 – VOICE, an HIV prevention trial evaluating two antiretroviral (ARV)-based approaches for preventing the sexual transmission of HIV in women – daily use of one of two different ARV tablets or of a vaginal gel – will be dropping one of the oral tablets from the study. The decision to discontinue use of tenofovir tablets in VOICE comes after a routine review of study data concluded that the trial will not be able to demonstrate that tenofovir tablets are effective in preventing HIV in the women enrolled in the trial. VOICE will continue to test the safety and effectiveness of the other oral tablet, Truvada[®], a combination of tenofovir and emtricitabine, and of the vaginal gel formulation of tenofovir.

Importantly, the review, which was conducted by the National Institute of Allergy and Infectious Diseases (NIAID)'s independent Prevention Trials Data and Safety Monitoring Board (DSMB), identified no safety concerns with any of the products being studied in VOICE.

VOICE – Vaginal and Oral Interventions to Control the Epidemic – involves 5,029 women at 15 trial sites in Uganda, South Africa and Zimbabwe. The trial is being conducted by the [Microbicide Trials Network](#) (MTN), an HIV/AIDS clinical trials network funded by the National Institute for Allergy and Infectious Diseases with co-funding from the *Eunice Kennedy Shriver* Institute for Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health.

The study was designed with five study groups: tenofovir gel, an inactive placebo gel, oral tenofovir, oral Truvada and an inactive placebo tablet. The women in each group (about 1,000) are asked to take their assigned study product daily. VOICE is the only trial evaluating the daily use of an ARV tablet – an approach called oral pre-exposure prophylaxis, or PrEP – and a vaginal gel in the same study. This design is important for determining how each product works compared to its control (placebo gel or placebo tablet) and which approach women prefer.

On September 16, 2011, the NIAID Prevention Trials DSMB reviewed VOICE study data for the period between Sept. 9, 2009, when the study began, and July 1, 2011. Based on this interim review, the DSMB determined that it was not possible to show whether oral tenofovir tablets were any better than a placebo for preventing HIV in the women assigned to that study group. The DSMB therefore recommended that the women randomized to the oral tenofovir tablet group discontinue their use of the study product. This recommendation does not apply to the women in the groups using either the tenofovir gel or oral Truvada tablets, or the corresponding placebos; the DSMB recommended that these four study groups continue in VOICE.

All VOICE participants will be informed about the decision to modify the study. Because the DSMB had no concerns about the safety of oral tenofovir, the process of discontinuing its use among the participants in that study group can proceed in an orderly fashion. Each of these participants will stop using the oral tenofovir tablets at their next scheduled clinic appointment. They will then return eight weeks later for a last set of tests and procedures before exiting the study. The participants will be provided with information about where they can receive HIV testing and counseling, contraception and other medical or support services as needed. Women in the oral tenofovir group who became HIV-infected and/or pregnant during VOICE and are enrolled in an MTN ancillary study may continue to participate in these studies.

The investigators, led by Zvavahera Mike Chirenje, M.D., of the University of Zimbabwe in Harare, and Jeanne Marrazzo, M.D., M.P.H., from the University of Washington in Seattle, U.S., expressed their disappointment that oral tenofovir did not reduce HIV infection in participants receiving it, but noted that the objective of the study was to answer questions about each of the approaches. Researchers don't know why the tenofovir tablet was not effective in the study's population – predominately women in their 20's (and younger) who may or may not be

-more-

married or in a committed relationship and are living in communities where HIV incidence is among the highest. Meanwhile, the team remains committed to completing the trial and to providing evidence on whether oral Truvada and/or tenofovir gel are effective in reducing the risk of HIV infection among young women.

The team is especially grateful to all of the VOICE participants, whose commitment to this trial has already helped gain insight about oral tenofovir tablets for preventing HIV among women. This information will have significant implications for a field that faces important decisions about the use of oral PrEP and in which particular populations it could have the most benefit.

No additional information about the independent DSMB's decision is available at this time. Once the study is completed, which is expected to be before the end of 2012, a full analysis of all data will be conducted.

A DSMB is an independent group of clinical research experts, statisticians, ethicists and often community representatives that provides additional oversight to a clinical study. A DSMB regularly reviews blinded data not available to the investigators or anyone else, while a clinical trial is in progress. Based on its review of interim data, a DSMB may, at any time, recommend that a trial, or part of a trial, be stopped if there are concerns about safety, compelling evidence for a product's effectiveness or if it becomes clear that the trial cannot show that a product is effective, a concept called futility.

Since the study began in September 2009, the NIAID Prevention Trials DSMB has conducted five periodic reviews of VOICE interim data. All reviews prior to the 16 September review indicated no concerns, and the DSMB recommended each time that the study continue, without changes. The next routine review of VOICE data by the DSMB will take place in mid-November of this year. This will be the sixth routine review and the third interim efficacy analysis of VOICE.

Globally, women account for 60 percent of adults with HIV in sub-Saharan Africa, where unprotected heterosexual intercourse is the primary driver of the epidemic. Young women are especially vulnerable. In southern Africa, young women are up to five times more likely to become infected with HIV than young men, and more than a quarter (26 percent) of all new global HIV infections occur in women aged 15-24. Women are twice as likely as their male partners to acquire HIV during sex. Although correct and consistent use of male condoms has been shown to prevent HIV, women are not always able to negotiate their use. Women desperately need methods for preventing HIV that they can control themselves. ARV-based prevention methods – as either a vaginal gel or an oral tablet – are promising approaches.

Oral tenofovir (tenofovir disoproxil fumarate), known by the brand name Viread[®], and Truvada, a combination tablet that contains tenofovir and emtricitabine, are both approved for the treatment of HIV when used in combination with other ARVs. Viread and Truvada are registered trademarks of Gilead Sciences, Inc., of Foster City, Calif., U.S. Both have been evaluated in clinical trials in different at-risk populations to determine if they can prevent HIV in people who are HIV-negative. Besides VOICE, only one other PrEP effectiveness trial is currently ongoing. The U.S. Centers for Disease Control and Prevention is testing the effectiveness of oral tenofovir taken daily for reducing the risk of HIV among 2,400 injection drug users in Thailand. Results are anticipated in 2012.

Tenofovir gel is a vaginal microbicide that contains the same active ingredient as the oral tablet formulation of tenofovir. Microbicides are products designed to prevent or reduce the sexual transmission of HIV when applied topically on the inside of the vagina or rectum. In 2006, Gilead assigned a royalty-free license for tenofovir gel to CONRAD, of Arlington, Virginia, and the International Partnership for Microbicides of Silver Spring, Maryland. In addition to VOICE, which is testing daily use of tenofovir gel, the FACTS 001 study plans to evaluate its use before and after sex in a large trial commencing soon in South Africa.

#

A Questions and Answers document about the modification of VOICE can be found at <http://www.mtnstopshiv.org/node/3622>
A summary of recent trial results of other PrEP studies can be found at <http://www.avac.org/ht/d/sp/i/326/pid/326>

About the MTN

The Microbicide Trials Network (MTN) is an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases (NIAID), part of the U.S. National Institutes of Health (NIH). The MTN brings together international investigators and community and industry partners who are devoted to reducing the sexual transmission of HIV through the development and evaluation of products applied topically or administered orally, working within a unique infrastructure specifically designed to facilitate the research required to support licensure of these products for widespread use.