



**CONTACT: Lisa Rossi**  
**PHONE : +1-412-641-8940**  
**+1-412-916-3315 (cell)**  
**E-MAIL: [rossil@upmc.edu](mailto:rossil@upmc.edu)**

**CONTACT: Michele Baum**  
**University of Pittsburgh**  
**PHONE: +1-412-647-3555**  
**E-MAIL: [baummd@upmc.edu](mailto:baummd@upmc.edu)**

**FOR IMMEDIATE RELEASE**

**Trial Suggests Tenofovir Gel is Safe for Daily Use, Finds Most Women Adhered to Study Regimens**  
**Results of Phase II study of ARV-based microbicide presented at international meeting in India**  
**bolster interest in latest approach**

**NEW DELHI, Feb. 25, 2008** – A vaginal microbicide that incorporates an antiretroviral (ARV) drug normally used to treat people with HIV is safe for sexually active HIV-negative women to use every day over an extended period, suggest results of a clinical trial of tenofovir topical gel. Moreover, most of the women who participated in the study conducted in India and the United States adhered to a regimen involving either daily or sex-dependent use of the gel, report researchers from the U.S. National Institutes of Health-funded Microbicide Trials Network (MTN) at Microbicides 2008, an international meeting taking place Feb. 24-26 at the Hotel Ashok in New Delhi.

The findings, presented today for the first time, are a significant boost to HIV prevention efforts focused on the potential of "next-generation" microbicides to curb infection rates in women. Globally, nearly half of those living with HIV/AIDS are women, and between 70 and 90 percent of all HIV infections in women are due to heterosexual intercourse. In India and many other parts of the world, even married women and women with steady partners are at risk.

In this Phase II study, called HPTN 059, researchers wanted to understand if tenofovir was safe to use every day for six months compared to its use prior to each act of sex, and if women were able to adhere, or follow, each regimen. Researchers found both approaches equally safe and women's adherence to product use similar. Interestingly, most participants also said they would be willing to apply gel, including daily, if one were found effective to prevent against getting HIV from their sexual partners.

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Microbicides are products designed to prevent the sexual transmission of HIV when applied topically on the inside of the vagina or rectum. Tenofovir gel is among a newer class of candidate microbicides that differ from early types because they have specific action against HIV. In addition, because tenofovir gel and similar products are longer acting, their use may not be required before each act of sex, which is not always practical or desirable for some women.

“Finding that daily use is both safe and feasible is important because we believe a daily approach may provide more sustainable protection against the virus in women who can’t always predict when they will have sex. Based on what we have learned we can proceed with greater confidence on a path that will answer whether tenofovir gel and other gels with HIV-specific compounds will be able to prevent sexual transmission of HIV in women when other approaches have failed to do so. It is a critical time for all of us engaged in HIV prevention, and I truly believe we are turning a corner,” said Sharon L. Hillier, Ph.D., professor and vice chair for faculty affairs, and director of reproductive infectious disease research in the department of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh School of Medicine, who is MTN principal investigator and led the study.

According to UNAIDS, women represent nearly half, or 46 percent, of the 33.2 million people living with HIV/AIDS worldwide, and they are more than twice as likely as men to acquire HIV through sexual intercourse, due to both biological and cultural factors. Although correct and consistent use of male condoms has been shown to prevent HIV infection, women often cannot successfully negotiate condom use with their male partners.

HPTN 059 involved 200 sexually active HIV-negative women: 52 were enrolled at the University of Alabama at Birmingham (UAB) in Birmingham, Alabama; 48 at Bronx-Lebanon Hospital Center, Bronx, New York; and 100 women entered the study at the National AIDS Research Institute in Pune, India. The mean age was 32 and 64 percent of the women were married. All but one of the women at the Indian site were married compared to 28 percent of the women at the two U.S. sites.

Once enrolled, women were randomly assigned to one of four groups: tenofovir gel applied daily; tenofovir gel applied up to two hours before sex; placebo gel (without an active drug) used every day; or placebo gel applied prior to sex. Because the tenofovir and placebo gels look the same, neither researchers nor participants knew who had been assigned to use which gel during the six-month study period. Women were assessed at one month, three months and six months. Throughout the study, participants received free condoms and HIV risk-reduction counseling as well as routine testing and treatment for sexually transmitted infections.

The study found no differences in liver, blood and kidney function between the groups of women using either regimen of tenofovir gel and the groups assigned to use placebo, nor were there differences in these safety measures between groups using daily gel and groups using gel with sex. Likewise, researchers report no

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statistical differences in the development of genital symptoms such as itching and burning, which are considered minor. One woman became pregnant and stopped gel use. No participants acquired HIV during the study.

Adherence to treatment was also similar. According to structured interviews, 80 percent of the women instructed to use gel within two hours of having sex said they complied with the regimen. Of the women in the daily-use groups, an average of 83 percent reported study gel use in the past week. The two most cited reasons women gave for not using gel was menstruation (41 percent) and forgetting (23 percent).

Overall, 41 percent of the women indicated there was nothing they disliked about using the gel and 39 percent said it was easy to use. Other attributes of the gel women identified included its potential for protecting against HIV (19 percent), its smell and appearance (14 percent) and that it made sex more pleasurable (12 percent). Thirty-two percent didn't like that the gel was messy, but none of the women said sex was made less pleasurable because of the gel.

Importantly, when asked if they would use the gel if it were found to help prevent people from getting HIV, 90 percent of the women who had been assigned to use the gel at the time of sex and 96 percent of the women who had been asked to use gel daily said yes.

"Women are definitely willing to use a gel to protect against sexual transmission of HIV. That's very encouraging," Dr. Hillier commented.

HPTN 059 also evaluated how the active ingredient in the gel was absorbed from the vagina into the blood and vaginal tissue; and looked at the effects of prolonged use on vaginal flora, the vagina's naturally protective population of microorganisms; and whether the activity of certain immune system molecules called cytokines could serve as a useful measure, or marker, for assessing the safety of microbicides. Results of these evaluations are not yet available.

HPTN 059 was conducted by the Microbicide Trials Network (MTN), a clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases (NIAID) with co-funding from the National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health (NIH). Prior to the establishment of the MTN, HPTN 059 study was led by the NIAID-funded HIV Prevention Trials Network (HPTN), from which the study gets its name.

At the site level, HPTN 059 was led by Smita Joshi, MBBS, in Pune, India; Jessica Justman, M.D., at Bronx-Lebanon Hospital; and Craig Hoesley, M.D., UAB.

In its pill form, tenofovir is a mainstay of one of the most widely used regimens for treating HIV. The active ingredient in tenofovir gel belongs to a class of anti-retroviral drugs called nucleotide reverse transcriptase inhibitors, which act against HIV by targeting a key enzyme the virus needs to copy itself before taking over a host cell. The topical gel form of tenofovir was not developed as treatment for HIV but as an approach to prevent the sexual transmission of HIV. Both oral and topical formulations were developed by

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Gilead Sciences, Inc., of Foster City, California, which assigned a royalty-free license for the topical gel to the International Partnership for Microbicides of Silver Spring, Maryland, and CONRAD, of Arlington, Virginia, in December 2006.

MTN will launch a series of other trials that will further evaluate the safety and adherence of tenofovir gel as well as look at its effectiveness for preventing HIV. Researchers will soon begin enrolling participants into MTN-002, the first trial of a candidate microbicide in pregnant women that seeks to understand the extent of drug absorption during pregnancy and the degree to which the active ingredient in tenofovir gel can be transferred to the fetus. Another trial, MTN-001, will be the first direct comparison of oral and vaginal gel preparations of tenofovir – looking at differences in drug absorption (systemically and locally) and adherence and acceptability of each approach separately and in combination. Finally, the VOICE Study (Vaginal and Oral Interventions to Control the Epidemic) will be the first effectiveness trial of a microbicide that women use every day instead of at the time of sexual intercourse. Moreover, VOICE will be the only trial evaluating two promising HIV prevention approaches in the same study: tenofovir gel and pre-exposure prophylaxis, or PrEP, an HIV prevention approach that involves daily use of oral anti-retrovirals.

Currently, tenofovir gel is being evaluated in a Phase IIb study being conducted at the Centre for the AIDS Programme of Research in South Africa (CAPRISA) in Durban. The study, known as CAPRISA 004, will enroll 980 women. Unlike VOICE, researchers are evaluating a dosing strategy timed around sexual intercourse.

Other microbicide products have been or are currently being tested in clinical trials, although none is yet approved or available for use by women.

In addition to Drs. Hillier, Justman, Joshi and Hoelsley, other authors of the HPTN 059 study presented at Microbicides 2008 are Elena Cyrus-Cameron, M.P.H., Family Health International, Research Triangle Park, North Carolina; Benoît Mâsse, Ph.D., Statistical Center for HIV/AIDS Research & Prevention at the Fred Hutchinson Cancer Research Center, University of Washington, Seattle; and Craig Hendrix, M.D., Johns Hopkins University, Baltimore, Maryland.

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**NOTE TO EDITORS:** For more information about HPTN 059 and/or to arrange interviews with the researchers, please contact Lisa Rossi at +1-412-916-3315. More information about HPTN 059 is available at <http://www.mtnstopshiv.org/node/167>. For information about other MTN studies, please go to [www.mtnstopshiv.org](http://www.mtnstopshiv.org).

**The Microbicide Trials Network** (MTN) is an HIV/AIDS clinical trials network established in 2006 by the Division of AIDS, National Institute of Allergy and Infectious Diseases (NIAID), part of the U.S. National Institutes of Health (NIH). The MTN brings together international investigators, community and industry partners who are devoted to reducing the sexual transmission of HIV through the development and evaluation of microbicides, working within a unique infrastructure specifically designed to facilitate research required to support licensure of topical microbicide products for widespread use. Based at the University of Pittsburgh and Magee-Womens Research Institute, MTN's principal investigator is Sharon Hillier, Ph.D. MTN's core operations are supported by a network laboratory at the University of Pittsburgh, a statistical and data management center housed within the Statistical Center for HIV/AIDS Research & Prevention at the Fred Hutchinson Cancer Research Center, and Family Health International, a global organization with expertise conducting clinical protocols. It receives its funding from three NIH institutes: NIAID, the National Institute of Mental Health and the National Institute of Child Health and Human Development. More information can be found at [www.mtnstopshiv.org](http://www.mtnstopshiv.org).