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FACT SHEET
Ongoing, Planned and Completed Trials of the Microbicide Trials Network

The Microbicide Trials Network (MTN) is an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases, with co-funding from the *Eunice Kennedy Shriver* 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. The MTN brings together international investigators and community and industry partners whose work is focused on the rigorous evaluation of promising microbicides – products applied inside the vagina or rectum to prevent the sexual transmission of HIV. These include multi-purpose products for preventing both HIV and unintended pregnancy and others to protect against HIV and different sexually transmitted infections.

MTN studies are designed specifically to support the potential licensure and regulatory approval of these products for populations particularly vulnerable to HIV. Because effectiveness of a product is also dependent on use, behavioral science is integrated throughout MTN's unique research portfolio. More than 25 clinical research sites on four continents have partnered with the MTN in the conduct of its clinical trials. Collectively, more than 12,000 research participants have taken part in MTN studies.

Ongoing and Planned Trials

Due to the COVID-19 pandemic and to protect study staff and participants, ongoing MTN studies are not screening or enrolling participants, while planned studies are on pause. Current participants continue to be followed by study teams to the extent this is both feasible and safe.

MTN-034/REACH (Reversing the Epidemic in Africa with Choices in HIV Prevention) **–** A Phase IIa trial that seeks to understand the HIV prevention needs and preferences of adolescent girls and young women in sub-Saharan Africa, who are among those most vulnerable to HIV. Specifically, REACH is evaluating how adolescent girls and young women use the monthly dapivirine vaginal ring and Truvada® as daily PrEP (pre-exposure prophylaxis), and their preferences for either or both approaches after using each for six months. REACH will also collect much needed information on the safety of the approaches in these populations. The study, which began in February 2019, will enroll 300 adolescent girls and young women ages 16-21 at four trial sites in South Africa, Uganda and Zimbabwe, and is expected to be completed late 2021.

MTN-035/DESIRE (Developing and Evaluating Short-acting Innovations for Rectal Use) – An acceptability, tolerability and adherence study of three placebo products for use in the rectum, including a douche, suppository and fast-dissolving rectal insert. The goal of the study is to help answer important questions about preferences for future rectal microbicide products. The products, which contain no active drugs, are currently being evaluated in 210 HIV-negative cisgender men, transgender men and transgender women who have sex with men at sites in Malawi, Peru, South Africa, Thailand and the U.S. Participants are asked to use each product for a 4-week period and report their use, likability and relative acceptability of the products. The study is expected to be completed mid-2020.

MTN-039 – A Phase I study launched in late 2019 that was designed to evaluate the safety and acceptability of a fast-dissolving rectal insert containing the antiretroviral (ARV) drugs tenofovir and elvitegravir, as well as the degree that each drug concentrates in rectal tissue. The study, the first ever of the tenofovir and elvitegravir insert used rectally, seeks to enroll 20 cisgender and transgender men and women at two sites in the U.S.

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MTN-042/DELIVER – A Phase IIIb open-label study designed to evaluate the safety and acceptability of the monthly dapivirine vaginal ring, which is under regulatory review, and Truvada as daily PrEP in pregnant women. The study, which launched in South Africa in early 2020, will enroll 750 women at different times during pregnancy who will use either the dapivirine ring or Truvada as PrEP until they deliver. Women will be followed for six weeks postpartum, and their babies will be followed for one year. Other trial sites are in Malawi, Uganda and Zimbabwe. The study is the first of the ring in pregnant women and will provide more insight about the safety of Truvada as PrEP during pregnancy, a time when women are at much greater risk of HIV.

MTN-043/B-PROTECTED – A Phase IIIb open-label study that will evaluate the safety and acceptability of the monthly dapivirine ring, which is under regulatory review, and Truvada as daily PrEP in women who are breastfeeding, a time of heightened vulnerability for acquiring HIV. The study will enroll up to 200 breastfeeding mothers and their 6- to 12-week-old babies. Women will use their assigned product – PrEP or the dapivirine ring – for three months and be followed for an additional two weeks. Researchers will assess how much drug from Truvada and the dapivirine ring passes into breastmilk and how much passes to the baby after breastfeeding, and will measure the effects, if any, this may have on their health. B-PROTECTED will be conducted at the same sites as the DELIVER study, which are in Malawi, South Africa, Uganda and Zimbabwe.

MTN-045 – A qualitative study that will enroll up to 400 couples in Uganda and Zimbabwe and aims to understand their views of and preferences for dual-purpose products that could feasibly prevent both unintended pregnancy and HIV infection. The study, which began early 2020, will help inform the design and delivery of dual-purpose products, including the role that male partners may play in the decision-making process.

Completed Trials with Results Pending

Vaginal Delivery Products

MTN-032 – A qualitative study to better understand women's use of the dapivirine ring in both ASPIRE (MTN-020), a placebo-controlled trial, and HOPE (MTN-025), an open-label extension study in which women were given the opportunity to use the ring for one year if they so chose. The study was conducted in two parts. Phase I involved 187 former ASPIRE participants who had been assigned to use the dapivirine ring and who took part in either a focus group or in-depth interview. Results, which were reported in 2018, found that women who didn't use the ring regularly feared their partners would oppose its use or feel it during sex. High adherers expressed altruistic motivations for ring use. Phase 2 involved 115 former participants who opted to enroll in HOPE, with results expected in mid- to late 2020. MTN-032 was conducted at six of the 15 clinical research sites for ASPIRE and HOPE.

MTN-036/IPM 047 – A Phase I open-label study of two formulations of a dapivirine vaginal ring intended to be used for 90 days – one with 100 mg of dapivirine and the other with 200 mg, as well as the monthly ring, which contains 25 mg of dapivirine. The study enrolled 49 women across two U.S. sites. Results, expected in late 2020, will provide information about the safety of the two 90-rings (which are also different silicone polymers) compared to the monthly ring and how much drug from each ring gets into vaginal tissue.

MTN-038 – A Phase I study of a 90-day vaginal ring containing tenofovir that was developed to protect women against both HIV and herpes simplex virus type 2 (HSV-2). The study assessed the safety of the ring and drug levels in tissue among 49 women at three U.S. trial sites. Results are anticipated in mid to late 2020.

MTN-041 – A qualitative study that took place in Malawi, South Africa, Uganda and Zimbabwe to understand community belief systems and attitudes that may affect women's perceptions about and potential interest in using the monthly dapivirine vaginal ring or daily PrEP during pregnancy and breastfeeding. The study involved group discussions with women, male partners and mothers and mothers-in-law of pregnant and breastfeeding women and interviews with community leaders, healthcare providers, midwives and traditional birth attendants, among others. The results, expected in mid-2020, will help inform implementation of the DELIVER (MTN-042) and B-PROTECTED (MTN-043) studies in pregnant women and breastfeeding women, respectively.

MTN-044/IPM 053/CCN019 – A Phase I study of a 90-day vaginal ring, containing dapivirine (200 mg) and the contraceptive hormone levonorgestrel, to prevent both HIV and unintended pregnancy in which the ring's safety and drug levels in tissue were assessed among 25 women in the U.S. The participants used a single ring for 90 consecutive days or cyclically for 90 days (taking it out every 28 days for 2 days.) Results are anticipated in late 2020.

Rectal Delivery Products

MTN-026 – A Phase I study that evaluated whether a gel containing dapivirine is safe for use in the rectum. The study, which enrolled 28 HIV-negative cisgender and transgender men and women at sites in Thailand and the U.S., will help determine whether further testing on the safety and acceptability of dapivirine gel as a potential rectal microbicide can be conducted in a larger population. Results are anticipated in mid-2020.

MTN-033 – A Phase I study that looked at the safety and distribution of dapivirine gel when administered rectally as a lubricant (without an applicator) to determine whether enough drug is delivered in the tissue to feasibly provide HIV protection. The study was conducted in the U.S. and enrolled 16 participants. Results are expected in mid-2020.

MTN-037 – A Phase I study that evaluated whether a microbicide gel called PC-1005 is safe for use in the rectum. The study, which included 12 HIV-negative cisgender and transgender men and women at two sites in the U.S., will help determine whether further testing of the safety and acceptability of PC-1005 as a potential rectal microbicide for preventing HIV and other sexually transmitted infections (STIs) can be conducted in a larger population. PC-1500 is the only product designed for vaginal and rectal use targeting HIV, herpes simplex virus (HSV) and human papillomavirus (HPV) simultaneously that has undergone Phase 1 testing to date. MTN-037 is the first study of PC-1005 used rectally. Results are anticipated by mid- to late 2020.

Completed Trials with Results

Vaginal Delivery Products

MTN-001 – A Phase II trial that looked at how tenofovir is absorbed in the body as either an oral tablet or a vaginal gel, as well as women's preferences or ability to adhere to the daily regimens of each approach. The study involved 144 women in South Africa, Uganda and the U.S., who used each product daily for six weeks, as well as the two together. The results of drug absorption studies, published in 2013, found the gel was associated with vaginal tissue drug levels more than 130-times higher than the oral tablet; the tablet was associated with a 56-times higher concentration of active drug in blood compared to the gel. Although self-reported adherence was very high (94 percent) and most women said they liked both products, drug serum concentrations indicated only 64 percent of the women took the tablets consistently.

MTN-002 – The first study of a candidate topical microbicide ever conducted in pregnant women, MTN-002 sought to understand whether tenofovir gel, which was being evaluated in trials to support its potential licensure, would be safe to use during pregnancy. The Phase I study involved giving a single dose of tenofovir gel to 16 healthy, HIV-negative women hours before they gave birth by scheduled Cesarean section. Results, reported in 2010, found only small amounts of drug were absorbed into the mother's bloodstream, amniotic fluid and umbilical cord (fetal) blood; and no serious side effects in either the mothers or their newborns. (See also MTN-008.)

MTN-003/VOICE (Vaginal and Oral Interventions to Control the Epidemic) – A Phase IIb study that tested the safety and effectiveness of two different HIV prevention approaches among 5,029 women in South Africa, Uganda and Zimbabwe: daily use of an ARV tablet (tenofovir or Truvada) or daily use of a vaginal gel (tenofovir gel). The study was conducted from 2009 to 2012. Results, first reported in 2013, found all three products were safe but none was effective; most participants did not use them daily as recommended. Young, unmarried women were least likely to use study products and the most likely to acquire HIV.

MTN-003B/VOICE B – Also known as the Bone Mineral Density Sub-study, VOICE B was an observational study in a subset of participants in VOICE designed to explore the potential effects, if any, that daily use of oral ARVs may have on bone health in HIV-negative women, and in particular, pre-menopausal women in Africa. VOICE B involved 518 women from Uganda and Zimbabwe who were assigned to one of the oral tablet regimens (oral tenofovir, oral Truvada or oral placebo) in VOICE. VOICE B found small decreases in bone mineral density among young women with higher adherence to the oral tablet tenofovir, findings that are consistent with previous studies, which resolved after stopping its use.

MTN-003C/VOICE C – Also known as the Community and Adherence Sub-study, VOICE C was designed to identify community-based factors and beliefs that may have influenced women's ability and willingness to use the products being tested in VOICE and was conducted in parallel with VOICE at a single site. Participants included 102 women enrolled in VOICE, as well as male partners, members of the site's Community Advisory Board (CAB) and community stakeholders. Results suggest women didn't use the products because of worries about side effects and the stigma associated with ARVs, which are used for treating people with HIV; and not knowing if they'd been assigned to use an active product or placebo.

MTN-003D/VOICE D – A behavioral sub-study of VOICE that aimed to understand women's actual and reported use of study products and sexual behavior during their participation in VOICE. Stage 1 involved 88 women who took part in individual in-depth interviews after exiting VOICE and before the trial's results were publicly reported. Stage 2 was implemented in response to VOICE results and involved 127 former participants who took part in in-depth interviews and/or focus group discussions after learning the results of blood tests indicating their actual patterns of product use during the trial. The most common themes that emerged were fears about the products and their side effects, which were primarily fueled by other participants, relatives and community members' negative attitudes about the products.

MTN-004 – A Phase I study that tested the safety and acceptability of VivaGel® (SPL7013 Gel) in HIV-negative women ages 18 to 24. The study, a collaboration with the NIH's Adolescent Trials Network (ATN) for HIV/AIDS Interventions, was conducted at two U.S. sites and one in Puerto Rico. Results, reported in May 2010, found VivaGel generally well-tolerated but less acceptable to use than the two placebo gels studied.

MTN-005 – An expanded safety and acceptability study of a non-medicated vaginal ring made of a silicone elastomer that enrolled 195 sexually active, HIV-negative women. The study was conducted at three sites – one in India and two in the United States.

MTN-008 – An expanded Phase I safety and drug absorption study of tenofovir gel used daily for seven consecutive days in women in their third trimester of pregnancy, and women who were breastfeeding. The study enrolled 90 pregnant women – 45 women at 37 weeks gestation and 45 women at 34 weeks gestation; and 16 women who were breastfeeding. MTN-008 was a follow-up study to MTN-002 and conducted at two U.S. sites. Results, first presented in 2013, indicated daily use of tenofovir gel in the third trimester of pregnancy was safe and well-tolerated, tenofovir did not accumulate in breast milk, and absorption of the drug in breastfeeding infants was low. (See also MTN-002.)

MTN-009 – Also called the HIV Drug Resistance Study, MTN-009 assessed the prevalence of HIV drug resistance in KwaZulu-Natal, South Africa. Results, published in 2013, found the prevalence of HIV drug resistance was 7.4 percent, with the majority of women with resistance having virus with the K103N mutation that confers resistance to most drugs in the class of ARVs called non-nucleoside reverse transcriptase inhibitors

MTN-011 – A Phase I study that aimed to determine the effect vaginal sex may have on drug absorption and activity of tenofovir gel. The study, which was conducted at two sites in the U.S., enrolled 24 couples. Study results, presented in 2014, showed that drug levels were highest when tenofovir gel was used one hour before and one hour after sex, suggesting that the timing of gel use relative to sex impacts the drug's absorption and activity.

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MTN-012/IPM 010 – A Phase I study that assessed the safety and tolerance of a vaginal microbicide containing the ARV drug dapivirine when applied topically to the penis of sexually abstinent men. Results, which were reported in 2012, found the gel safe and well-tolerated.

MTN-013/IPM 026 – A Phase I safety and drug absorption study that tested 28-day use of vaginal rings containing either dapivirine, maraviroc, or the two ARVs combined, and was conducted among 48 women at three U.S. sites. The study was the first clinical trial of a vaginal ring containing maraviroc, and the first to test a vaginal ring with two active drugs. Results, reported in 2014, found the ring was safe in women and evidence of dapivirine in cervical tissue and blood. In addition, laboratory tests of tissues samples showed that dapivirine was able to block HIV infection, though levels of maraviroc were not sufficient to have a similar effect.

MTN-014 – A Phase I study that examined drug absorption patterns in both rectal and vaginal tissue when a reduced glycerin formulation of tenofovir gel was applied either vaginally or rectally. The study enrolled 14 women at a U.S.-based clinical research site. Results, reported in 2015, demonstrated that when tenofovir gel was applied into the vagina, a low amount of active drug was distributed to the rectum and, similarly, when the gel was applied into the rectum, a low amount of active drug was distributed to the vagina.

MTN-015 – A long-term, observational study that was designed to track the nature of HIV progression and treatment response among women who acquired HIV while taking part in an MTN "parent study" of an ARV-based HIV prevention product. In total, MTN-015 enrolled 479 women from one of four MTN studies (HPTN-035, MTN-003/VOICE, MTN-020/ASPIRE and MTN-025/HOPE), beginning in 2013. Results reported thus far suggest there are no differences in the progression of HIV or in responses to treatment (e.g., development of drug resistance) among women who received an ARV-based prevention product and those who received a placebo.

MTN-016/EMBRACE (Evaluation of Maternal and Baby Outcome Registry After Chemoprophylactic Exposure) – An observational study and data registry to understand the effects, if any, the use of ARV-based HIV prevention products may have on pregnancy and infant outcomes. The study enrolled women who unintentionally became pregnant while participating in the MTN-003/VOICE, MTN-020/ASPIRE or MTN-025/HOPE studies (and then immediately stopped use of the study product), as well as their babies. Women and their babies from MTN-002 and MTN-008 were also included. In total, MTN-016 has collected data on 460 women and 413 infants. Among the study's findings, researchers report no significant differences in pregnancy and infant outcomes between women in the ASPIRE study who were using the dapivirine ring at the time they became pregnant and women from the placebo group who became pregnant, supporting additional safety studies of the dapivirine ring throughout pregnancy. (See MTN-042/DELIVER.)

MTN-020/ASPIRE (A Study to Prevent Infection with a Ring for Extended Use) – was a Phase III study to determine whether a vaginal ring containing the ARV drug dapivirine is a safe and effective method for protecting against the sexual transmission of HIV when used by women for a month at a time. ASPIRE enrolled 2,629 sexually active HIV-negative women ages 18-45 and was conducted between 2012-2015 at 15 clinical research sites in Malawi, South Africa, Uganda and Zimbabwe. Results, reported in 2016, found HIV risk was reduced by 27 percent overall and no safety concerns. HIV risk was cut by more than half (56 percent) in women older than 21, who also appeared to use the ring most consistently. Results of an exploratory analysis reported at AIDS 2016 found the level of HIV protection for those who appeared to use the ring most consistently was at least 56 percent and as high as 75 percent or more with near perfect use. The ring was developed by the International Partnership for Microbicides (IPM), which conducted another Phase III trial, The Ring Study, in parallel with ASPIRE.

MTN-023/IPM 30 – A Phase I safety study of the dapivirine vaginal ring in adolescent girls that was conducted at six U.S. research sites from 2013 to 2016 in collaboration with the National Institutes of Health-funded Adolescent Medicine Trials Network (ATN) for HIV/AIDS Interventions. The study enrolled 96 girls ages 15-17 at six U.S. sites who were randomly assigned to use either the dapivirine ring or a placebo ring each month for six months. Results, which were presented at IAS 2017, found no differences in safety outcomes between the dapivirine ring and the placebo ring. Ring acceptability and adherence to ring use were also high.

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MTN-024/IPM 31 – A Phase I safety study of the monthly dapivirine ring in 96 post-menopausal women conducted at three sites in the U.S. Results, which were published in 2019, found the ring was safe and well-tolerated.

MTN-025/HOPE (HIV Open Label Prevention Extension) – An open-label follow-on trial to ASPIRE (MTN-020) in which former ASPIRE participants were offered the opportunity to use the dapivirine ring (there was no placebo) in the context of a study designed to collect additional information about safety and how women would use the ring knowing that it was shown to reduce the risk of HIV in ASPIRE. HOPE enrolled 1,456 women at 14 sites in Malawi, South Africa, Uganda and Zimbabwe. Women were free to accept the ring or not, and to change their minds at any time during the study. Results, which were presented at IAS 2019, found that ring was well-tolerated, consistent with the safety profile seen in ASPIRE, and the majority of women from ASPIRE chose the ring being offered. Measures of adherence also indicated they were willing to use the ring to protect themselves against HIV.

MTN-027 – A Phase I study, which along with its companion study, MTN-028, was one of the first clinical trials to test a type of ARV called an integrase inhibitor as a potential microbicide. MTN-027 looked at the safety of three vaginal rings: one that contained the integrase inhibitor MK-2048; a second ring containing vicriviroc (MK-4176), which is a CCR5-receptor antagonist; and a third ring that contained both active drugs. Results, reported in 2019, found the rings to be safe and acceptable among the 48 women in the study from two U.S. sites.

MTN-028 – A Phase I trial that evaluated two vaginal rings, each containing a different dose of the same two ARV drugs – a CCR5-receptor antagonist called vicriviroc (MK-4176) and an integrase inhibitor, MK-2048. MTN-028 sought to understand the optimal doses of MK-4176 and MK-2048 needed to achieve concentrations of drug in tissue that could feasibly provide HIV protection. According to results, reported in 2019, both doses of rings were safe and well tolerated. MK-4176 and MK-2048 were detectable in plasma and tissues in higher amounts in the higher dose ring compared to the lower dose ring. MTN-028 and MTN-027 were the first clinical studies of an integrase inhibitor as a potential microbicide.

MTN-029/IPM 039 – The first study of its kind involving the dapivirine vaginal ring in breastfeeding women, MTN-029/IPM 039 found that very low concentrations of dapivirine released from the ring into the vagina were absorbed by breastmilk in lactating women. Sixteen women who were no longer breastfeeding but were still producing breast milk were enrolled into the study and used the ring for 14 consecutive days. Results, which were reported at IAS 2017, supported additional studies of the dapivirine ring in breastfeeding women. (See MTN-043/B-PROTECTED.)

MTN-030/IPM 041 – A Phase I trial of a vaginal ring containing the ARV drug dapivirine and the contraceptive hormone levonorgestrel that assessed the ring's safety as well as absorption patterns of dapivirine and different dosages of levonorgestrel in vaginal tissue and in blood. MTN-030/IPM 041, which was conducted at two U.S. sites, found the ring was well-tolerated with no safety concerns. The study represents an important first step toward developing a product for women that could both protect against HIV and prevent unintended pregnancy. (See also MTN-044 and MTN-038.)

Rectal Delivery Products

MTN-006 (RMP-02/MTN-006) – A Phase I study involving 18 HIV-negative men and women that was designed to determine whether the vaginal formulation of tenofovir gel is safe to use in the rectum, and through novel laboratory studies, if the gel prevents HIV infection in rectal tissue sampled from study participants. Results, reported in 2011, found HIV infection was significantly inhibited in rectal tissue sampled from participants who used tenofovir gel daily for one week. Because some participants experienced gastrointestinal side effects, researchers subsequently reformulated the gel to include less glycerin. The study was conducted in collaboration with the Division of AIDS Integrated Pre-Clinical/Clinical Program for HIV Topical Microbicides of the National Institute of Allergy and Infectious Diseases. (See also MTN-007 and MTN-017.)

MTN-007 – A Phase I follow-up study to RMP-02/MTN-006 that found rectal use of a reduced glycerin formulation of tenofovir gel safe and acceptable among the 60 men and women who took part in the study at three U.S. sites. Based on results, which were first reported in 2012, researchers proceeded with a Phase II trial of reduced glycerin tenofovir gel, MTN-017. (See also MTN-006 and MTN-017.)

MTN-017 – A Phase II trial designed to evaluate the rectal safety, drug absorption and acceptability of a reduced glycerin formulation of tenofovir gel, as well as oral Truvada, at sites in Peru, South Africa, Thailand and the U.S., including Puerto Rico. The study enrolled 195 cisgender men and transgender women who have sex with men. Results, which were reported February 2016, found the gel was safe to use, with participants preferring to use the gel around the time of sex as opposed to daily.

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More information about the MTN is available at www.mtnstopshiv.org.

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