

FACT SHEET About Microbicides

Fast Facts

- Microbicides are products applied inside the vagina or rectum that would protect against HIV through sex. This is important, because the most common way people acquire HIV is through condomless vaginal or anal sex with someone who is HIV positive. Unlike condoms, microbicides are controlled by the user, not by a sexual partner. And unlike other biomedical approaches that rely on the systemic delivery (throughout the body) of antiretroviral (ARV) drugs, microbicides deliver drugs directly to the site of potential infection.
- Vaginal microbicides are being designed in many forms, including fast-dissolving films and inserts, and rings that slowly release an active ingredient during its use, which could be a month or longer. One product, a monthly vaginal ring containing the ARV dapivirine, is under regulatory review. Rectal microbicides are also being studied, as douches, lubes and inserts – products that may conform to behaviors already practiced around the time of anal sex. Some microbicide formulations are also being developed and tested as multi-purpose products for preventing both HIV and unintended pregnancy and others for preventing both HIV and different sexually transmitted infections.
- The only approved biomedical prevention method that currently exists is an approach called pre-exposure prophylaxis (PrEP), which involves taking a daily ARV pill, most commonly Truvada. But not everyone wants to or can take a daily pill. A microbicide could feasibly offer an additional HIV prevention option. Just like contraceptives to prevent unintended pregnancy, the more options available, the more likely one can and will be used.
- Nearly 1.6 million people are newly diagnosed with HIV annually – about 5,000 every day – with approximately one-third of these instances occurring among people ages 15-24, and nearly half among cisgender women. In sub-Saharan Africa, young women aged 15–24 years are twice as likely to be living with HIV compared with men of the same age. Across the globe, gay men and other men who have sex with men and transgender people continue to be especially vulnerable to HIV.

What will it take to discover a safe and effective microbicide?

Drug development is a long and arduous process, often taking up to 20 years for a product to be approved for general use. Thousands of potential compounds may be considered during drug discovery but only the most promising are subjected to rigorous laboratory and animal studies, and fewer still make it to trials with people.

Clinical trials are carried out in several phases under the oversight of regulatory and research authorities and according to strict ethical and scientific guidelines. Phase I trials are designed to evaluate safety in a small number of people and for short periods, say, one to two weeks. If results of a Phase I study suggest the product is safe, investigation may progress to a Phase II trial to track its safety in more people over longer periods of time. Phase IIb and III trials are much larger studies that are designed to determine a product's effectiveness, as well as to gather more safety information. They can take up to four years to conduct, and their results weigh heavily in a regulatory agency's decision whether to approve the product for widespread use.

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Vaginal Microbicides

The idea for a microbicide-like product was first proposed about 30 years ago by reproductive health specialists and advocates who recognized the need for female-controlled HIV prevention methods. One of the first products considered was the spermicide nonoxynol-9, but clinical trials found it neither safe nor effective against HIV. Trials of other so-called first-generation microbicides also yielded disappointing results. These included products that were meant to strengthen natural defenses in the vagina or create a barrier to protect target cells. Researchers have since focused on products that incorporate ARV drugs.

The first ARV-based microbicide in clinical trials was a vaginal gel containing tenofovir. While in 2010, the CAPRISA 004 study showed that tenofovir gel reduced cisgender women's risk of HIV infection by 39 percent when used before and after sex, these results were not confirmed in either the VOICE or FACTS 001 studies. In both of these studies, tenofovir gel was not effective due to poor adherence. In VOICE, women were asked to use the gel daily. The FACTS 001 study tested the gel used before and after sex.

Researchers have met with greater success with vaginal rings, flexible products that fit inside the vagina and provide sustained delivery of drugs over a period of time. In 2016, two large clinical trials involving women in sub Saharan Africa – [ASPIRE](#), conducted by the Microbicide Trials Network (MTN), and The Ring Study, conducted by the International Partnership for Microbicides (IPM), a non-profit organization that developed the dapivirine ring – found the monthly dapivirine vaginal ring was well-tolerated and helped reduce the risk of HIV by approximately 30 percent. Higher levels of protection were seen in women who used the ring most regularly. Based on these results and those of several supporting studies, IPM is seeking regulatory approval of the ring for use by women 18 and older. If approved, it would be the first biomedical prevention option specifically for cisgender women – and the first long-acting method. In parallel, MTN is conducting safety studies of the ring in adolescent girls and young women as well as in pregnant and breastfeeding women so that national programs can consider expanded approval to include these populations should the ring be approved in the first place.



A vaginal ring containing tenofovir, developed by CONRAD, is also under study. Because tenofovir also acts against herpes simplex virus type 2 (HSV-2), the tenofovir ring could feasibly protect against both HIV and HSV-2. CONRAD's tenofovir ring is designed to be used for 90 days. A 90-day dapivirine ring is also being developed by IPM. Both organizations have developed rings that include an active anti-HIV drug (tenofovir or dapivirine) along with a contraceptive hormone for dual protection against both HIV and unintended pregnancy.

In addition to vaginal rings, researchers are also exploring vaginal inserts and paper-thin quick-dissolving vaginal films that after insertion would melt away and disperse active drug to protect cells in the vagina. Both are in the early phases of clinical testing.

Rectal Microbicides

Although the majority of microbicide research has focused on products to prevent HIV through vaginal sex, anal sex is practiced by people of all genders and sexualities around the world. According to some estimates, the risk of becoming infected through anal sex is 20 times greater than vaginal sex because the rectal lining, the mucosa, is thinner and much more fragile than the lining of the vagina.

Early rectal microbicide studies at the MTN evaluated the use of vaginal tenofovir gel in the rectum, finding that it caused gastrointestinal side effects. Researchers then tested a reformulated version of the gel with less glycerin and found the reformulated gel to be safe and acceptable. MTN has since completed a Phase II study of the reduced glycerin formulation of tenofovir gel among cisgender men and transgender women who engage in anal intercourse – the first ever of a rectal microbicide. The study, MTN-017, took place in Peru, South Africa, Thailand and the United States. Results, announced in early 2016, found the gel was safe, with participants preferring to use it around the time of sex compared to daily use.

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Several more rectal microbicide studies at the MTN have been completed and are anticipating results in 2020. Another key study fully enrolled and completing follow-up, [MTN-035, or DESIRE](#) (Developing and Evaluating Short-acting Innovations for Rectal Use), is evaluating acceptability, tolerability and adherence to a placebo douche, suppository and rectal insert among 210 cisgender men and transgender men and women who engage in anal intercourse. DESIRE is the first study to systematically examine potential methods for HIV prevention from receptive anal sex and will help answer important questions about preferences for future microbicide products. The study is taking place in Malawi, Peru, South Africa, Thailand and the United States.

Other rectal-related research programs underway include DREAM (Delivery of Rectal Enema as Microbicide), which is exploring the delivery of a rectal microbicide as a single dose enema, and PREVENT (Griffithsin-based Rectal Microbicides for Prevention of Viral Entry), which is addressing the need for a non-ARV based rectal microbicide.

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About 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. Based at Magee-Womens Research Institute and the University of Pittsburgh, the MTN brings together international investigators and community and industry partners whose work is focused on the development and rigorous evaluation of promising microbicides – products applied inside the vagina or rectum that are intended to prevent the sexual transmission of HIV – from the earliest phases of clinical study to large-scale trials that support potential licensure of these products for widespread use. More information about the MTN is available at <http://www.mtnstopshiv.org>.

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