



## What are microbicides?

Microbicides are products being developed to protect healthy people from acquiring HIV during sex. Most microbicides contain antiretroviral (ARV) drugs—the same types of drugs successfully used to treat HIV/AIDS—to reduce the risk of infection when they are used consistently.

Some microbicides are being designed for women as vaginal products in forms such as long-acting rings and on-demand vaginal inserts and films. Rectal microbicides are being developed for men and women, and some microbicides in development are designed for both vaginal and rectal use.



The nonprofit International Partnership for Microbicides (IPM) is focused on developing microbicides to protect women from HIV during vaginal sex with a male partner. Safe and effective microbicides could have an important impact as part of a comprehensive prevention strategy that includes condoms, daily oral ARV pills (known as pre-exposure prophylaxis or PrEP), future injectables and, one day, a vaccine. There will be no single solution to ending the epidemic—stopping HIV will require a variety of options.

## Why microbicides?

HIV/AIDS is a leading cause of death in women ages 15–49 worldwide. In sub-Saharan Africa, nearly 60% of all new HIV infections occur among women and girls.

Although a number of prevention methods exist, they are not doing enough to stop the virus's spread. Heterosexual sex is the primary mode by which HIV spreads in developing countries. Women are at higher risk of infection due to a

combination of biology and gender inequities. For example, it is often not possible for women to negotiate condom use with their partners. In addition, although daily oral PrEP is highly effective when used consistently, some women are not able, or choose not to, use it.

Microbicides would help meet the needs of different women at different times in their lives—and support them to protect their sexual and reproductive health on their own terms.

## What has microbicide research shown us?

**Early microbicides:** The earliest microbicides were not based on ARVs and showed no protection against HIV in several studies that took place from 1994 to 2009.

**Tenofovir gel:** In 2010, a vaginal gel containing the ARV tenofovir showed proof-of-concept for microbicides. However, subsequent studies did not confirm the product's efficacy due to low product use.

**Dapivirine ring:** In 2016, the dapivirine ring, developed by IPM, became the first microbicide and the first long-acting method shown to reduce HIV risk in two Phase III clinical trials. The ring, which is designed to slowly release the ARV dapivirine, is self-inserted and replaced monthly.

### How effective is the dapivirine ring?

The ring was shown to reduce HIV infections by 35% in The Ring Study, led by IPM, and by 27% in ASPIRE, led by our partner the US National Institutes of Health-funded Microbicide Trials Network. No safety concerns were seen with long-term use of the product. The two studies enrolled nearly 4,600 women ages 18–45 in four African countries.

Results from two subsequent open-label extension studies, DREAM and HOPE, showed increases in ring use and modeling data suggested greater risk reduction—by over 50% across both studies—compared to the Phase IIIs. Although these modeling results are limited due to the lack of a placebo comparison group, they indicate an encouraging trend.

### What are the next steps for the ring?

Following a positive regulatory opinion from the European Medicines Agency in 2020 and a recommendation from the World Health Organization in 2021, IPM is seeking country regulatory approvals for the dapivirine ring's use in sub-Saharan Africa, where the need is urgent. The ring is also under review by the US Food and Drug Administration.

In addition, studies are underway to better understand the safety and use of the ring as well as daily oral PrEP among groups at especially high risk for HIV: adolescent girls and young women ages 16-21, pregnant women and breastfeeding women. A study of the ring is also planned to complement existing efficacy data and to better understand the product's efficacy among women ages 18-25. Together, findings from these and other studies will provide insights into how the ring could fit into the lives of these key groups.

## Why do we need multiple options?

Because it is the only way to bring the epidemic under control. One method will not work for everyone, and no product is perfect. Offering a range of prevention choices—including long-acting and woman-controlled methods—is critical to ensuring that a woman can choose one that meets her individual needs and circumstances.

Efforts to expand women's HIV prevention options include multipurpose products now being developed that would prevent both unintended pregnancy and HIV—and sometimes other sexually transmitted infections (STIs), too. Other potential methods include long-acting injectable ARVs, and in earlier stages of development, implants, long-acting oral PrEP, rectal and dual-compartment gels, and vaccines.

## How are safety and efficacy studied?

All microbicide candidate products go through rigorous laboratory screening and testing to ensure an adequate safety profile before being studied in humans.

Clinical trials are carried out sequentially, first to determine the safety of a product (no significant side effects) and then to test its efficacy. Initial safety trials involve small numbers of volunteers who participate under carefully controlled clinical conditions. Larger safety trials involving more volunteers over longer periods are then conducted to collect additional safety data, also under controlled conditions.

Efficacy trials are then performed to assess whether the microbicide reduces HIV risk. These trials involve large numbers of volunteers (hundreds to thousands) and need to be conducted in locations where new HIV infections occur at a high rate. This allows researchers to assess the difference in infection rates between volunteers who use the active microbicide and those who use a placebo, which contains no active drug. IPM will make its microbicides available in trial countries, if found effective and approved.

## What ethics guide clinical trials?

All clinical trials, including microbicide trials, must be conducted according to international and national regulatory and ethics guidelines to protect participants' well-being, and guarantee the ethical and scientific integrity of the results.

Informed consent is the cornerstone of ethical trial conduct. Clinical research teams must ensure that all volunteers in a microbicide trial have freely given their informed consent based on a clear understanding of the trial, including the risks and benefits of participating. The informed consent process must be consistent with International Conference on Harmonisation Good Clinical Practice and local country guidelines. Informed consent is an ongoing process that requires periodic and ongoing discussions with participants to ensure their continued understanding of the trial.

As part of the standard-of-care guidelines for HIV prevention trials, participants receive ongoing HIV and STI risk-reduction counseling, condoms, pre- and post-HIV test counseling, family planning counseling and treatment for curable STIs that are identified. Participants are also referred for support, care and treatment in the event that they become infected with HIV or require medical attention for other conditions.



*A research center staff member demonstrates how to insert a vaginal ring at a journalist training in Edendale, South Africa.*

## How are local communities involved?

In countries where clinical trials are conducted, IPM and its research partners implement broad-based programs and events to engage community members. Information about microbicides and clinical trials is provided in local languages to trial participants and key stakeholders, including local officials, women's groups, medical professionals, the media, traditional leaders, ministries of health and others. Ongoing training and support for those involved in the clinical trial process is also provided to clinical investigators, research scientists, nurses, counselors, community health workers and project management staff.

## Conclusion

Expanding women's options with safe and effective microbicides promises to be a major public health accomplishment. Realizing that potential requires continued investment and political will to deliver promising innovations to the women who urgently need them.