

Microbicide Overview



INTERNATIONAL
PARTNERSHIP FOR
MICROBICIDES

What are microbicides?

Microbicides are products being developed to protect healthy people from becoming infected with HIV during sex. Most microbicides contain antiretroviral (ARV) drugs. Multiple clinical trials have shown that ARVs—the same types of drugs successfully used to treat HIV/AIDS—can prevent 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 both 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 on the epidemic as part of a comprehensive prevention strategy that includes condoms, daily oral ARV pills (known as pre-exposure prophylaxis or PrEP) 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 the leading cause of death globally in women ages 15-44, and young women in sub-Saharan Africa are twice as likely as young men to become infected with HIV.

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, not all women will be able to take daily oral PrEP, which is highly effective when used consistently and is being made available in some countries.

Microbicides would help meet the needs of different women at different times in their lives—and allow 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 1994-2009.

Tenofovir gel: In 2010, a vaginal gel containing the ARV tenofovir was shown to reduce women's HIV risk by 39% when used before and after sex, providing proof-of-concept for microbicides. Two subsequent studies did not confirm those findings, however, 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 help reduce HIV risk in late-stage 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?

Two Phase III studies—The Ring Study, led by IPM, and ASPIRE, led by our partner the US National Institutes of Health-funded Microbicide Trials Network—found that the monthly ring was well-tolerated and reduced HIV infections among women in the trials by about 30% overall. HIV risk reduction was likely greater among participants who used the ring at least some of the time. HIV risk was reduced by 40% among women over 21; no risk reduction was seen in women under 21 overall, likely due to low product use.

In 2019, results from two subsequent open-label extension studies, DREAM and HOPE, showed increases in ring use and modeling data suggest 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 we hope to see continue if the ring is approved.

What are the next steps for the ring?

A study called REACH began in February 2019 to assess the safety of and adherence to the ring and PrEP among young women and adolescents ages 16-21 in Africa. Together, findings from these and other studies will provide insights into the adherence challenges to both methods and identify ways to help address them.

IPM is applying to regulators to license the product for use in countries where women face the highest risk for HIV. The ring is currently under review by the European Medicines Agency for use in developing countries, with submissions to the US Food and Drug Administration, South African Health Products Regulatory Authority and other national regulatory authorities in Africa planned.

Why do we need multiple options?

Because it is the only scenario that can bring the epidemic under control. One method will not work for everyone. We need a range of new self-initiated prevention tools women can choose from that fit within the context of their lives.

To that end, researchers are developing multipurpose products designed to prevent both unintended pregnancy and HIV—and sometimes other sexually transmitted infections (STIs), too. Other prevention methods in clinical studies include long-acting injectable ARVs, implants, on-demand 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 test the ability of the microbicide to reduce 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 clinical 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 local research partners implemented 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

Offering microbicides to women in developing countries promises to be one of the great public health accomplishments of our generation. Realizing that potential requires continued investment and political will to deliver promising innovations to the women who urgently need them.