

Microbicide Overview

Why microbicides?

HIV/AIDS ranks among the world's most devastating diseases. About 35 million people worldwide are living with HIV/AIDS, and almost 36 million already have died from AIDS-related causes. Each day, over 6,000 more women, men and children become infected with HIV, the virus that causes AIDS. Globally, nearly 17 million children, the majority of whom live in sub-Saharan Africa, have lost one or both parents due to HIV (UNAIDS, 2013).

Women bear a high burden of the epidemic as primary caregivers for the ill and because of their heightened risk of infection due to biological, economic and social vulnerabilities. HIV/AIDS is the leading cause of death globally in women ages 15-44, particularly in sub-Saharan Africa. Although a range of prevention strategies exists, they are not enough to stop the spread of HIV, especially among women. Heterosexual sex is the primary mode by which HIV spreads in developing countries. Many women are unable to negotiate condom use with their male partners and abstinence is not an option for women who are married, who want children or who are at risk of sexual violence. This is why we urgently need new HIV prevention strategies like microbicides that women can use themselves.

What are microbicides?

Microbicides are medical products being developed to protect healthy people from becoming infected with HIV during sex. Most microbicides contain antiretroviral (ARV) drugs that attack the virus at one of a number of points in the HIV life cycle. ARV medicines have extended and saved millions of lives across the globe — and these drugs are now being adapted to protect healthy adults from becoming infected with HIV. Multiple clinical trials have shown the powerful potential of antiretroviral-based HIV prevention.

Some microbicides are being designed for women as vaginal products, and others in early development would be rectal products that both men and women could use. Microbicides for women could come in many forms, including vaginal gels used around the time of sex and long-acting monthly rings. A safe and effective microbicide could have a profound impact on the epidemic as part of a comprehensive prevention strategy that includes condoms, PrEP and, one day, a vaccine. The International Partnership for Microbicides (IPM) is focused on developing microbicides to protect women from HIV during sex with a male partner.

When might we have a vaginal microbicide?

There are just two microbicide products currently in late-stage clinical trials: tenofovir vaginal gel, to be used before and after sex, and IPM's monthly dapivirine vaginal ring. Each product must show efficacy in two Phase III clinical trials to be licensed. See below for clinical trial details and time lines for:

Tenofovir gel

CAPRISA 004: In 2010, the CAPRISA 004 study in South Africa showed that a vaginal microbicide gel containing the ARV tenofovir reduced women's risk of HIV infection by 39 percent when used once before sex and again afterward. In a surprise finding, tenofovir gel also reduced by half the number of HSV-2 infections, the cause of most genital herpes.

VOICE (MTN-003): In 2013, the VOICE trial, led by the US National Institutes of Health (NIH)-funded Microbicide Trials Network (MTN), found that tenofovir gel did not reduce the risk of HIV infection in women when used daily. The trial took place in South Africa, Uganda and Zimbabwe.

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FACTS 001 (Follow-On African Consortium for Tenofovir Studies): This confirmatory trial of tenofovir gel in South Africa, initiated in 2011, uses the same dosing strategy as CAPRISA 004. FACTS 001 expects results in early 2015.

SUMMARY: While CAPRISA 004 showed that tenofovir gel reduced study participants' risk of HIV infection, the VOICE trial found that the gel did not reduce the risk in women due to low adherence to the daily dosing regimen used in that trial—underscoring the challenge of developing and delivering a product women can and want to use. Currently, the field awaits the results of FACTS 001, which uses the same before-and-after sex dosing regimen as the CAPRISA 004 trial. FACTS 001 will confirm whether tenofovir gel is an effective HIV prevention tool for women.

Dapivirine ring

IPM 027 (The Ring Study) and MTN 020 (ASPIRE):

IPM 027 (The Ring Study), led by IPM and currently under way, is designed to evaluate whether IPM's dapivirine ring is safe and effective in preventing HIV infection in women when used for one month at a time. Launched in 2012, The Ring Study is taking place in South Africa and Uganda among 1,950 women, with results expected by 2016.

MTN 020 (ASPIRE) is evaluating the efficacy and safety of IPM's dapivirine ring and is being led by our partner, the MTN. ASPIRE was initiated in 2012, and is taking place in Malawi, South Africa, Uganda and Zimbabwe among 2,629 women, with results expected in late 2015.

Together, these parallel “sister” studies, along with several smaller safety studies, will determine the ring's efficacy and long-term safety. Pending all study results by 2016, IPM, the product developer and regulatory sponsor, will seek regulatory approval for the ring's licensure.

SUMMARY: For the first time, a microbicide ring is being tested in large-scale safety and efficacy trials for HIV prevention. Because IPM's ring is designed to deliver an ARV continuously over one month, it has the potential to help address the challenge of adherence and help ensure effectiveness.

Why is product choice important?

As recent oral PrEP and microbicide research has shown, only when an ARV-based prevention product is used consistently can it be effective. Stopping HIV's spread requires a toolkit of products that address individual needs and preferences. Some women may prefer taking an ARV pill (oral PrEP) every day; some may prefer an on-demand gel used before and after sex; while others may prefer a long-acting discreet product like a vaginal ring that they replace only monthly. It's about giving women options, because a product that best suits a woman's needs and preferences is much more likely to be used consistently and correctly.

An advantage of microbicides is that they can be formulated at an affordable cost in multiple delivery methods — from short-acting gels and films to long-acting rings. Microbicides deliver the active ARV drug locally where it is needed with low systemic absorption. Microbicides can also be used discreetly, giving women who may not be able to discuss HIV prevention options with their partners the ability to protect their own health,

Combination products: Microbicides combining two or more ARVs in a single product that target HIV at different points in the life cycle could increase the level of protection, as is the case with ARVs used in treatment. The first combination microbicide to be tested in a clinical trial is IPM's dapivirine-maraviroc vaginal ring. The trial, conducted in partnership with MTN, found the ring to be safe, well-tolerated and acceptable to women. An optimized formulation is expected to be ready for preclinical testing in 2015.

MPTs: Also in development are several multipurpose prevention technologies, designed to prevent against unintended pregnancy and HIV infection — and sometimes other sexually transmitted infections as well. IPM's 90-day dapivirine-contraceptive ring is anticipated to enter clinical trials in 2015.

How are microbicides tested for safety and efficacy?

All microbicide candidate products must go through a rigorous program of laboratory screening and testing to ensure that they have an adequate safety profile before being tested in humans. Once a microbicide candidate satisfactorily passes these tests and additional safety tests in animals, it can be advanced through a series of human clinical trials.

Clinical trials are carried out sequentially, first to determine the safety of the product (no significant side effects occurred) and then to test its efficacy (the ability of the product to prevent HIV infection). Initial safety trials involve small numbers of women who participate under carefully controlled clinical conditions. Larger safety trials involving a wider range of women over longer periods are then conducted to gain broader safety data.

Efficacy trials are then performed to test the ability of the microbicide to prevent HIV infection. These trials involve large numbers (hundreds to thousands) of women, and need to be conducted in locations where new HIV infections are occurring at a high rate. This allows researchers to better assess the difference in infection rates between those women who use the active microbicide and those who use a placebo (similar to the microbicide, but not containing any active drug). If significantly fewer women become infected in the group that used the microbicide, then researchers know that the microbicide helps to prevent HIV infection.

What ethical standards guide clinical trials?

All clinical trials, including microbicide trials, must be conducted according to international and national regulatory and ethics guidelines to protect trial 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 participants in microbicide trials have freely given their informed consent based on a clear understanding of the trial, including the risks and benefits of trial participation. 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.

In addition, as part of the standard of care guidelines for clinical trials, participants are provided with ongoing HIV and sexually transmitted infection (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 any other condition.

How are local communities involved?

In countries where clinical trials are conducted, IPM and its local research partners have implemented broad-based programs to engage community members. Information about microbicides and clinical trials is provided in local languages not only to trial participants but also to 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 testing process — clinical investigators, research scientists, nurses, counselors, community health workers and project management staff — is also provided.

Developing safe and effective microbicides for women in developing countries promises to be one of the great public health accomplishments of our generation.

How will women's access to microbicides be ensured?

Once developed and approved for use, microbicides must be made widely available and affordable. Historically, it can take decades for the benefits of scientific innovation to reach the developing world. IPM and the broader microbicide field are committed to expediting widespread availability and access of an effective product, reaching those most in need first. Ensuring access to microbicides is a responsibility that must be shared by trial sponsors, research teams, donors, multilateral and bilateral agencies and national governments.

Conclusion

Microbicides will be critical to any comprehensive response to HIV/AIDS — one that takes into account the disproportionate impact of the epidemic on women — and a much needed tool in promoting women's sexual and reproductive health and well-being. Science has shown the powerful potential of ARVs to prevent HIV infection and save lives— now realizing that potential requires continued financial resources and political will to deliver promising innovations to the women who need them. Offering safe and effective microbicides for women in developing countries promises to be one of the great public health accomplishments of our generation.