

Why Do We Need a Diverse Pipeline of Microbicides for HIV Prevention?

Where we are today: Proof that ARV prevention works against HIV

After nearly 20 years of research on microbicides, the HIV prevention field demonstrated in recent years that antiretroviral (ARV) drugs—the same types of drugs used successfully to treat HIV—could help prevent HIV infection.

- **Microbicides:** The proof-of-concept study, CAPRISA 004, found that a vaginal gel containing the ARV drug tenofovir prevented 39% of new HIV infections among women when used before and after sex. Although two subsequent trials of the gel — VOICE (daily dosing) and FACTS 001 (before-and-after sex dosing)— did not find the gel to be effective due to challenges related to product adherence, subsets of women who were able to use the gel had a reduced risk of infection. Long-acting products, some of which are already in clinical trials, may be more practical options.
- **PrEP:** Multiple studies of products called pre-exposure prophylaxis (PrEP) have shown that *oral* ARVs, when used consistently, can reduce the risk of HIV infection in certain populations. However, achieving high adherence among young women has been a central challenge in oral PrEP studies to date. This highlights the need for products that fit into the context of women's lives.
- **Vaccines:** Looking toward the future, it is hoped that an effective HIV vaccine will complement microbicides and PrEP, along with other interventions in the HIV prevention toolkit.

Where we need to go: Working toward more effective and acceptable products

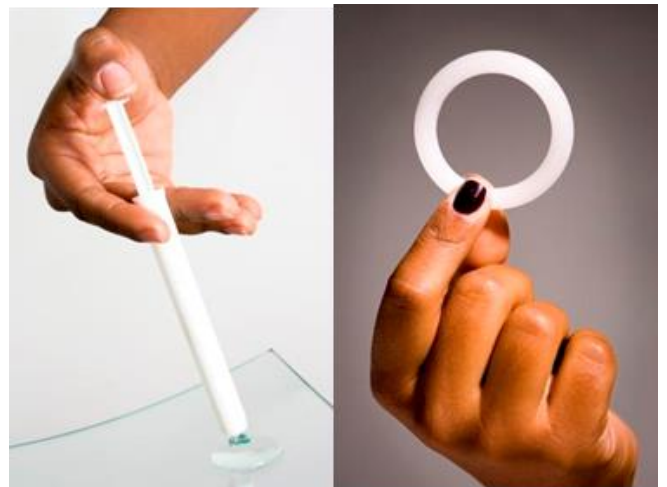
A robust pipeline based on new drugs and optimized formulations can build upon current successes by advancing products with potentially higher efficacy.

Product options

A microbicide, no matter how effective, will not prevent HIV unless women find it acceptable and easy to use in their everyday lives. Therefore, we need multiple and complementary HIV prevention tools — from rings to films and beyond — that fit women's needs to ensure they will be widely used and ultimately increase the real-world effectiveness of these products.

Resistance: Expanding the range of effective drugs

When resistance to anti-malarial drugs emerged a few years after their introduction, we learned how important it is to sustain investment in active product pipelines to ensure infectious diseases are kept at bay over time.



The ability of HIV to develop resistance to existing ARV drugs is also a concern, particularly because HIV treatment is long-term. A pipeline that contains a diverse range of drugs that have multiple mechanisms of action may also help prevent HIV over time.

In addition, some ARV drugs currently used in HIV treatment are now being used for HIV prevention, which could increase the chance that HIV may become resistant to one or more ARVs. A microbicide pipeline that includes classes of drugs used solely for the prevention of HIV will help reduce such a risk.

Because it takes more than a decade for prevention products to go through clinical trials and reach regulatory approval, research and development on additional drugs must happen now.

Moving microbicide research forward

Through our six licensing agreements with pharmaceutical partners that allow the development of eight different ARV compounds as microbicides, IPM is developing a range of products to address the urgent health risks that women around the world face every day:

- **The monthly ring:** Our most advanced product is the monthly dapivirine ring, developed to provide women with long-acting protection from HIV. The vaginal ring, now in two Phase III efficacy and safety studies in multiple countries in Africa, is designed to release the ARV drug dapivirine over the course of a month to provide women with a self-initiated and easy-to-use tool to protect their own health.
- **Combination products:** IPM is also pioneering the development of combination products, including the first microbicide to combine two types of ARVs in a single product. As the state-of-the-art for current HIV/AIDS treatment regimens, combination ARVs may offer greater protection against HIV than a single drug alone.
- **New types of ARVs:** IPM surveys emerging data and consults with scientific partners to advance promising ARVs with alternative mechanisms of action and high potency. For example, IPM is prioritizing a new gp120 inhibitor that can target HIV directly and acts early in the virus' lifecycle, which may have important benefits for HIV prevention.

Microbicide product development is an iterative and challenging process, continuously informed and driven by new findings. It is crucial to build on recent progress in HIV prevention by pursuing an active product pipeline that is based on a range of drugs and dosage forms to produce additional — and more effective — solutions that will prevent HIV over time and help to end the epidemic.