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 films and tablets. Rectal microbicides are also being developed for both men and women.

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.

Tenofovir gel: In 2010, a vaginal gel containing the ARV tenofovir was shown in the CAPRISA 004 study to reduce women’s risk of HIV infection by 39 percent when used before and after sex, providing proof-of-concept for microbicides. Two subsequent studies were unable to confirm those findings, however, due to low product use.

Dapivirine ring: In 2016, the monthly dapivirine ring, developed by IPM, became the first microbicide to confirm efficacy in two late-stage clinical trials. The ring, which slowly releases the ARV dapivirine over the course of a month, is also the first long-acting HIV prevention method.

How effective is the dapivirine ring?
Two Phase III “sister” studies — The Ring Study, led by IPM, and ASPIRE, led by our partner the Microbicide Trials Network — showed that the monthly ring safely reduced HIV infections in women by about one-third overall. Exploratory analyses show the ring cut HIV risk by 56 percent with consistent use, and potentially by 75 percent or more with near-perfect use.

What are the next steps for the ring?
Two open-label extension studies, DREAM and HOPE, are now ongoing to provide the ring to former Phase III participants, and to help us understand if use will increase now that the product’s safety and efficacy are known. A different study planned for 2017 will focus on young women and adolescents ages 16-21 in Africa, and assess the safety of and adherence to the ring and PrEP. Findings from all these studies will provide insights into the adherence challenges to both methods and identify ways to help address them.
Given the ring’s promise for many women at high risk, IPM is pursuing regulatory approval for its use in developing countries, with the first submissions planned for 2017. First approvals could be received in late 2018.

**Why do we need multiple options?**

Existing HIV prevention options work for some, but not all, women. Women need a range of new self-initiated prevention tools they can choose from that fit within the context of their lives. Having multiple options is not simply a best-case scenario — it is the only scenario that can end the epidemic.

To that end, several microbicides containing multiple ARVs are in earlier stage development as are multipurpose products designed to prevent both unintended pregnancy and HIV infection — and sometimes other sexually transmitted infections (STIs), too. Other prevention methods in early-stage clinical studies include long-acting injectable ARVs, rectal gels, broadly neutralizing antibodies 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 women who participate under carefully controlled clinical conditions. Larger safety trials involving a wider range of women over longer periods are then conducted to collect broader safety data, also under controlled conditions.

Efficacy trials are then performed to test the ability of the microbicide to prevent HIV infection. These trials involve large numbers of women (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 women 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.

In addition, 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 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 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 safe and effective microbicides to women in developing countries promises to be one of the great public health accomplishments of our generation. Realizing that potential will require continued financial resources and political will to deliver promising innovations to the women who urgently need them.