Microbicides for HIV Prevention
An Introductory Factsheet
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For more basic fact sheets in this series on emerging HIV prevention strategies visit www.avac.org/intro.

What is a microbicide?

Microbicides are substances that can be applied in the vagina and/or rectum to reduce the risk of HIV infection via sexual exposure. There are no licensed microbicides available today. They could come in a number of forms, including creams, gels, films, vaginal and rectal suppositories, and intra-vaginal rings which release an active ingredient over a few weeks or months.

What is the status of microbicide research?

Two candidates have shown some effect in lowering the risk of HIV acquisition.

Dapivirine Ring: In February 2016, two trial teams announced results of the effectiveness and safety of a vaginal ring containing the antiretroviral drug, dapivirine. Both trials found modest levels of overall protection. This is the first time that two trials of a microbicide showed highly comparable results.

The results are exciting, but potential access to the ring is still several years away.

1% tenofovir gel: This candidate showed modest efficacy in a trial whose data were released in 2010. Subsequent trials did not confirm this finding. It is unlikely that this product will move forward.

What did the dapivirine ring trials find?

The two sister trials are known as The Ring Study, which was conducted by the International Partnership for Microbicides, and ASPIRE, which was conducted by the Microbicide Trials Network (MTN). The two studies together recruited over 4,500 women in total from Malawi, South Africa, Uganda and Zimbabwe.

Both studies found the ring was safe and reduced rates of HIV acquisition by about one-third. The results of the Ring Study showed a 31 percent reduction in HIV, and the ASPIRE results showed a 27 percent reduction. Both trials analyzed residual drug levels in the rings returned by participants and in participants' blood samples. Results provided imprecise but helpful measures of adherence—how consistently participants wore the ring. Among women over age 21, who appeared to keep the ring in consistently throughout the month, HIV acquisition rates were even lower than the overall percentages above. Further data analysis from the ASPIRE trial, shared in July 2016, showed similar findings. Researchers identified four different levels of adherence, from non-use to near-perfect use. Among women with the most regular use rates, HIV risk was cut by more than half across all analyses, and in some, by 75 percent or more.

How do these data relate to previous research?

In previous trials of both daily oral PrEP and 1% tenofovir gel, older women also reported higher levels of adherence. Younger women in the trials used the products less frequently. This doesn’t mean the products wouldn't work in young women’s bodies if used correctly and consistently. It means that, in the trial context, the products did not work in young women’s lives.

Resources and links

AVAC (www.avac.org)
CONRAD (www.conrad.org)
International Partnership for Microbicides (www.ipmglobal.org)
International Rectal Microbicide Advocates (www.rectalmicrobicides.org)
Microbicide Trials Network (www.mtnstopshiv.org)
Population Council (www.popcouncil.org)
What happens now?

For now, the dapivirine ring is only available in research settings. Two open-label extension (OLE) studies are underway. They will offer the dapivirine ring to all former trial participants for 1 year. From these trials researchers will gather additional information on the ring’s safety, how women use it once they know it can reduce their risk of HIV, and how adherence affects HIV protection. ASPIRE’s OLE trial is named HOPE, the RING study’s OLE is named DREAM. The MTN is planning other studies to help answer additional questions beyond the scope of the OLE. Meanwhile, the product developer of the ring, IPM, is compiling all the evidence to apply for licensure to expand access beyond research sites.

What is the status of tenofovir gel studies?

1% tenofovir gel is the antiretroviral drug, tenofovir (TFV) used in gel form as a vaginal microbicide. Three trials have explored its efficacy. The first, CAPRISA 004, found evidence of modest benefit. Two subsequent trials, VOICE and FACTS 001, found no overall evidence of protection. A recently completed open-label study in South Africa, CAPRISA 008, provided access to tenofovir gel through family planning clinics to participants in CAPRISA 004 who were HIV-negative. While the study of TFV gel may not continue, CAPRISA 008 demonstrated that integrating HIV prevention strategies into reproductive services was feasible and acceptable to participants and resulted in good adherence, similar to the level achieved in a clinical trial setting. This could be useful to policy makers and health care providers scaling up oral PrEP.

New data, shared in July 2016, emphasize the importance of the vaginal microbiome, the environment of microorganisms that exist in the vagina. Data suggest some “bad” bacteria may increase women’s susceptibility to HIV by either weakening the vagina’s natural sperm- and germ-fighting environment, metabolizing preventive drugs, or by increasing inflammation. Other “good” bacteria such as lactobacillus seem to help stave off HIV. More research is needed to better understand good and bad bacteria and how to leverage them for HIV prevention.

What about rectal microbicides?

The first Phase II rectal microbicide gel study, MTN 017, released results in February 2016. This open-label trial looked at a tenofovir gel with a reduced-glycerin formulation, inserted with an applicator, and compared daily use with “on-demand” use (before and after sex). A third arm of the study added oral Truvada to the regime. All 195 MSM and transgender women cycled through each arm of the study for eight weeks. All methods delivered safe and effective results. Participants preferred on-demand usage to daily usage. Data will soon be published on the acceptability of the applicator. Early feedback from community consultations suggest the applicator is not acceptable and the product may not go forward to an efficacy trial.

The Adonis phase I study, poised to launch soon, will look at the safety and distribution of dapivirine gel administered with an applicator vs a “coital simulation device” (science-speak for dildo). Dapivirine was chosen for its high potency and its proven efficacy via vaginal ring delivery. Adonis will help answer whether a rectal microbicide delivered like a lube—instead of via an applicator—can deposit enough drug in the right place to potentially provide protection from HIV. Another study looking at the safety of dapivirine as a rectal gel is slated to launch mid-2016. Other early-stage studies are testing additional ARV-based gels for rectal use as well as the non-ARV-based product, Griffithsin.

What other candidate microbicides are under study?

Numerous candidates are in the early phases of development—see more at www.avac.org/trials/microbicides.

- **New delivery mechanisms**: Basic and preclinical work is underway with films and fast-dissolve vaginal inserts that contain a variety of ARVs. This work is in early human trials or preclinical (laboratory-based) research.
- **Non-ARV-based options**: Research on non-ARV-based candidates includes zinc acetate and Griffithsin.
- **Multipurpose prevention technologies**: There is a growing interest in developing tools that could provide contraception and protection against STI’s, including HIV. Vaginal rings are one candidate, as are injectables, films and fast-dissolving vaginal inserts. See www.avac.org/multipurpose-prevention-technologies.

About AVAC | AVAC uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of new HIV prevention options as part of a comprehensive response to the pandemic. More at www.avac.org.