



# Microbicides

This fact sheet provides basic information on microbicides, one of the options being tested now as part of the effort to identify additional tools to reduce the risk of HIV transmission.

## **What is a microbicide?**

The term microbicide refers to substances being studied that could be used in the vagina and/or rectum to reduce the risk of HIV transmission during sex. The first data to show that a microbicide can be effective at reducing the risk of HIV infection were released in July 2010. The CAPRISA 004 trial found that 1% tenofovir gel reduced HIV-negative women's risk of HIV infection via vaginal sex by an estimated 39 percent overall.

The large majority of microbicide candidates in testing today are formulated with antiretroviral (ARVs) drugs. The current effectiveness trials (see back) are exploring tenofovir gel. Tenofovir is one of the ARVs that people living with HIV use as treatment. The idea is that ARVs formulated as a microbicide and applied in the vagina or rectum might be able to block HIV activity at the site of exposure, thereby preventing infection. Studies are closely monitoring women who use such products and go on to become HIV infected, in order to learn whether gel use affects drug resistance.

In addition to microbicides that contain an active ingredient meant to block HIV activity directly (like ARV-based candidates), there is also research into other candidates, like those that may act as a physical barrier at the mucosal lining of the vagina or rectum. Microbicides could come in a number of forms, including creams, gels, films, slow-release vaginal rings, enemas and suppositories that could be used vaginally or rectally.

The first microbicides tested (those initially tested in large-scale trials from 1996 through 2008) were known as broad spectrum agents, meaning that they were intended to provide broad coverage against several STIs but were not specific to HIV. Researchers hoped that they would work by disrupting the virus membrane or by boosting the vagina's natural defenses. These products (e.g., Carraguard, BufferGel, Pro2000) were tested in large-scale trials and shown to be ineffective, and in the case of Nonoxynol-9 (spermicide tested for HIV protection) that it could potentially increase vulnerability to HIV by disrupting the vaginal epithelium.

## **Why is research being done to identify a microbicide?**

The goal of a microbicide is to reduce the risk of HIV infection at the site of sexual exposure (vagina or rectum). Microbicides research was inspired by grassroots advocacy that called for options that women at high risk for HIV could use and control themselves in preventing HIV and other sexually transmitted infections. Although research has been focused primarily around vaginal microbicides, this has been broadened to include research and development of rectal microbicides that men and women can use to protect themselves during anal sex.

## **How will we know if microbicides work?**

Every HIV biomedical prevention candidate goes through an extensive series of evaluations, first in laboratory and animal studies and then in humans. The animal studies provide preliminary information about the safety and effectiveness of the candidate. Only those candidates that appear safe in animals are considered for human testing. Efficacy data from animals can also be used to inform decisions about whether to test a candidate in humans. However, studies in animals cannot give a clear answer about whether a strategy will reduce HIV risk in humans. In microbicide animal studies, scientists control exactly when the drug is taken and when the animal is challenged with the virus. Trials in humans provide information about how the strategy works in situations where product usage may not be 100 percent consistent and the timing of exposure is frequently not known.

Microbicide candidates that meet criteria in laboratory and animal studies are moved into small safety studies in humans (Phase I trials). Candidates that appear to be safe and meet certain criteria are then tested in expanded safety studies (Phase II trials). Some of the candidates that complete these stages with positive results are moved into large-scale efficacy or effectiveness trials, which may be called Phase III, Phase IIb, test-of-concept, or proof-of-concept trials. There are technical reasons why some trial designs are called efficacy and others are effectiveness studies. Both terms refer to trials that look at whether a candidate reduces the risk of

HIV infection. For simplicity, the term efficacy is used below.

The details of these large-scale efficacy studies vary, but the design of microbicide efficacy trials is similar to that of most HIV prevention trials. These trials enroll healthy, HIV-negative people, most commonly in communities where researchers have conducted preparatory work to learn about the rates of risk behaviors and incidence. Each participant receives a basic prevention package including treatment for sexually transmitted infections, condoms, and behavior change counseling. [Unfortunately, needle exchange is not provided in all of the efficacy trials involving injection drug users, and this area is receiving continued attention from advocates and activists.] Some of the participants are randomly assigned to receive the experimental microbicide, while the other participants receive a placebo, a product that is indistinguishable from the experimental microbicide and has no effect on the body. No participant knows whether he or she is receiving the candidate microbicide or placebo. All participants are counseled at every study visit that they can't assume they will be protected by the microbicide and that they cannot know whether they have received the experimental microbicide or the placebo.

Over the course of the trial period, some participants get infected even though they are being counseled and receiving prevention services. This is consistent with what we know about the AIDS epidemic: even with information and services, not everyone can protect himself or herself all the time.

At the end of the trial, researchers compare the rates of new infections in the participants who received the experimental microbicide and in those who received the placebo. If there are significantly fewer new infections in the experimental microbicide group, that is, if the difference is greater than that which can be attributed by chance, this suggests that the microbicide is beneficial.

#### **Where are microbicide trials taking place?**

There are nearly 20 clinical trials of experimental microbicides currently underway, in countries around the world, with a concentration in East and Southern Africa. Visit [www.avac.org/globalmap](http://www.avac.org/globalmap) for a map of ongoing microbicide and other biomedical HIV prevention trials.

#### **Who is participating in microbicide research?**

Like other HIV prevention strategies, microbicide trials are conducted among different populations including heterosexual women and gay men and other men who have sex with men. Women at high risk for HIV make up the largest number of trial participants in ongoing microbicide trials. Both men and women participate in safety studies for rectal use of microbicides, and men participate in studies to assess penile safety.

#### **When are results expected?**

Results from CAPRISA 004, the first large-scale study of an antiretroviral-containing microbicide, were announced July 2010. The trial found that 1% tenofovir gel reduced HIV-negative women's risk of HIV infection via vaginal sex by an estimated 39 percent overall. The trial also found that 1% tenofovir gel reduced risk of HSV-2 infection by over 50% among women in the trial who were not infected HSV-2 at the beginning of the trial. CAPRISA 004 follow-up studies are being planned. In 2013, the VOICE study (MTN 003), another large-scale trial, is scheduled to release results. VOICE is evaluating three different strategies to prevent HIV in women: 1% tenofovir gel and two different daily oral PrEP regimens. For more information on the way forward in the development and testing of 1% tenofovir gel, visit [www.avac.org/tenofovirgel](http://www.avac.org/tenofovirgel). There are also other ARV-based microbicides in pre-clinical and early clinical studies (for the complete list visit [www.avac.org/trials](http://www.avac.org/trials)).

Visit [www.avac.org](http://www.avac.org) for more on microbicides, including resources formerly available at [www.microbicide.org](http://www.microbicide.org).

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