



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.

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.

What is a microbicide?

The term microbicide refers to topical substances being studied that could be used in the vagina and/or rectum to reduce the risk of HIV transmission during sex. There are several ways in which a microbicide might provide this protection. It might contain an active ingredient that blocks HIV activity directly, or it may act as a physical barrier at the mucosal lining of the vagina or rectum. These could include creams, gels, films, slow-release vaginal rings, enemas and suppositories that could be used vaginally or rectally. The first effective microbicides may use just one mechanism of action. Later microbicides, however, will likely combine two or more mechanisms of action to make them more effective.

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.

The large majority of microbicide candidates in testing today are formulated with antiretroviral (ARVs) drugs. The current effectiveness trials (see overleaf) are exploring tenofovir gel. Tenofovir is one of the ARVs that people living with HIV use as treatment. The hope 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.

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 infectious 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 potential exposure to HIV 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

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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 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, are scheduled to be announced at AIDS2010 in Vienna in July 2010. 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: tenofovir gel and two different PrEP regimens that consist of taking oral ARVs on a daily basis. There are also other ARV-based microbicides in pre-clinical and early clinical studies.

Visit www.avac.org/trials for more on ongoing and completed microbicide trials.

Visit www.avac.org for more on microbicides, including resources formerly available at www.microbicide.org.

Founded in 1995, AVAC is an international, non-profit organization that uses education, policy analysis, advocacy and community mobilization to accelerate the ethical development and eventual global delivery of AIDS vaccines and other new HIV prevention options as part of a comprehensive response to the pandemic. For more information, visit www.avac.org.