

# Rethinking the Ethical Roadmap for Clinical Testing of Microbicides:

*Report on an International Consultation*

Prepared by  
the Global Campaign  
for Microbicides



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## Microbicide Basics

### What is a microbicide?

The word microbicide (mi-KRO'-bi-sid) refers to a range of products that share a common characteristic: the ability to prevent the sexual transmission of HIV and other STD pathogens when applied topically in the vagina or rectum. These products do not yet exist, but they are now being developed and tested with large human populations in clinical trials. Future microbicides could be produced in many forms—gels, creams, suppositories, films, or in sponges or vaginal rings that slowly release the active ingredient.

### When will microbicides be available?

To create a safe, effective product, scientists are now pursuing more than two dozen product leads. So far, 16 have proven safe and effective in animals and are being tested in people. With sufficient investment in the field, a successful microbicide could be on the market by the end of the decade.

### Would a microbicide eliminate the need for condoms?

No. When used consistently and correctly, male or female condoms are likely to provide better protection against HIV and STDs than microbicides. But for those who cannot or will not use condoms—and in particular, for women whose partners refuse to use condoms—microbicides will save lives and could have a substantial impact on the HIV epidemic. A mathematical model projects that if even a small proportion of women in low-income countries used a 60 percent efficacious microbicide in half the sexual encounters where condoms are not used, 2.5 million HIV infections could be averted over 3 years.

### Who is working on microbicide research and development?

To date, virtually all microbicide research has been conducted by nonprofit institutions, universities, and small biotech companies. The work has been primarily funded by charitable foundations and government grants. Public funds have contributed to microbicide development through support for basic science research, social and behavioral research, and support for clinical trial infrastructure. Large pharmaceutical companies have not significantly invested in microbicide development. As a classic "public health good," microbicides might yield tremendous benefits to society, but the profit incentive is low for private investment.

*(continued on inside back cover)*

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### **How does a microbicide work?**

There are four basic mechanisms of action by which various candidate microbicides may work: (1) Killing or inactivating pathogens-some microbicides work by breaking down the surface or envelope of the virus or pathogen; (2) Strengthening the body's normal defenses-the body has several naturally occurring defense mechanisms that a microbicide may be able to supplement or enhance. *Lactobacillus*, for example, is a naturally occurring, "good" bacteria that helps protect the vagina by maintaining its acidic environment. This natural acidity helps foster an inhospitable environment for many pathogens, including HIV. Thus, the idea of developing a microbicide that supports the lactobacilli in performing this function is one potential mechanism of action being explored; (3) Inhibiting viral entry-some microbicides bind to viruses and bacteria to prevent them from binding to and infecting healthy cells. (4) Inhibiting viral replication-some candidates are being developed from the anti-retroviral drugs that HIV positive people use to lower the amount of virus in their bodies. Formulated as gels or creams, these drugs may be able to suppress replication of any HIV that enters the vagina or rectum during sex. If so, they could substantially lower the odds that the microbicide user will become infected.

Eventually, microbicide products will probably combine several of these mechanisms of action.

### **How are microbicides tested?**

Any new drug is thoroughly researched in the laboratory and in animals before it is tested on people. In clinical trials, human participants test candidate microbicides to determine first, whether they are safe and, second, whether they are effective. In Phase 1 safety trials, the candidate product is used by a small number of volunteer participants for a limited period of time, with close monitoring to see if the product causes irritation or other adverse reactions. If it appears to be safe, it is tested by a larger number of volunteers in a Phase 2 safety trial. Phase 1 and Phase 2 microbicide trials enroll women in both industrialized and developing countries. The Phase 3, or effectiveness trial compares two groups-those who receive the microbicide plus condoms and those who receive a placebo plus condoms. The placebo looks just like the drug being studied but does not contain the active ingredient.

### **Does participating in a trial increase someone's risk of HIV?**

Participants do not increase their risk of becoming HIV infected as a result of being in the trial. In fact, many reduce their risk as a result of receiving trial-provided condoms and condom counseling in their own language. Some women will nonetheless become infected during the trial because-despite assistance and counseling-they are unable to insist on consistent condom use with their partners. Women in both arms of a Phase 3 trial generally have fewer HIV seroconversions than women in the general community because of the risk reduction efforts offered as part of the trial. Every effort is made to ensure that women understand that they should not count on the test product to protect them from infection-because its effectiveness is unknown-and that using condoms is the best way to protect themselves.

### **What is the Global Campaign for Microbicides, and what is its role in clinical trials?**

The Global Campaign for Microbicides is a broad-based international movement of advocates working to expand access to new and existing user-controlled methods of HIV prevention. The Global Campaign is endorsed by 200 NGOs worldwide, 55 of whom serve as active Campaign partners. One of the Global Campaign's core goals is to ensure that as the science proceeds, the rights and interests of trial participants, users, and communities are fully represented and respected. It is committed to negotiating the difficult line between urgency of the HIV epidemic and maintaining rigorous ethical standards in the development of microbicide products. The Campaign offers resources, assistance, and support to advocates and communities working to become active, well informed participants in this process. Fact sheets, documents, and newsletters can be downloaded at [www.global-campaign.org/download.htm](http://www.global-campaign.org/download.htm).





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