

# MICROBICIDE PRODUCT RESEARCH AND DEVELOPMENT



## THE POPULATION COUNCIL'S MICROBICIDES PROGRAM

New HIV prevention methods are urgently needed; worldwide, 2.7 million individuals are infected each year. To help stop the spread of HIV and other sexually transmitted infections (STIs), the Population Council is developing new, user-controlled prevention methods called microbicides that will allow women and men to protect themselves from infection. The Council is also developing microbicide/contraceptive combinations, which will allow women to prevent unintended pregnancy as well as HIV and STIs. These products, formulated as gels, rings, or other delivery vehicles, are being designed to deliver promising active pharmaceutical ingredients (APIs) to the site where protection is needed, which results in lower systemic absorption and fewer side effects.

**The Council's comprehensive approach to microbicides development covers the entire product development lifecycle—from basic science to clinical testing and behavioral research, to product introduction and public education.**

At the Council's Center for Biomedical Research in New York City, our researchers are studying the **basic science** of HIV transmission to discover novel ways to stop the virus. All the microbicide technologies in the **product development** pipeline are potentially multipurpose with activity against at least one STI in addition to HIV. A robust **field research** program increases our understanding of how women and men may use these products.

Strong regulatory and intellectual property strategies ensure the products we develop are safe, effective, and affordable. And a world-class panel of experts from the academic, non-profit, and industry sectors provides guidance and feedback on our efforts.

## BASIC SCIENCE: DISCOVERY

To better understand how to stop infection from occurring, Council researchers are studying the biological mechanisms of HIV transmission. The dendritic cell, a type of white blood cell, plays a critical role in driving HIV infection in T cells. Innovative strategies are being tested for their ability to activate mucosal dendritic cells *in vitro* and *in vivo* to suppress virus growth while boosting immunity. Because infection with herpes simplex virus (HSV) increases the risk of HIV transmission, researchers are studying whether HSV-induced changes in dendritic cell and T-cell function facilitate HIV spread across the mucosal surfaces of the body. The Council also explores how effectively novel APIs limit dendritic cell-driven HIV infection in mucosal tissues (in the presence or absence of other STIs) since this effectiveness is critical to advancing promising microbicide strategies.

## PRODUCT DEVELOPMENT: GELS

The Council has been at the forefront of gel-based microbicide research for two decades. The Council's first lead candidate microbicide, Carraguard®, an aqueous gel containing carrageenan (a natural polymer obtained from seaweed), was conceived, developed, and advanced through clinical trials by Council staff.

It was the first microbicide candidate to complete a Phase 3 microbicide efficacy clinical trial among a general population of women as planned and with no safety concerns. It was also the first microbicide trial to supplement self-reported gel use with an objective assay to measure use.

Today, Council scientists are developing next-generation microbicide gels that contain one or more APIs formulated in carrageenan (CG): MIV-150/ZA/CG gel, which contains two effective antiviral agents—MIV-150 (an enzyme inhibitor developed by Medivir that prevents HIV-infected cells from producing new virus) and zinc acetate (an antiviral agent with activity against HIV and HSV)—that would provide two mechanisms of action against HIV and HSV-2 and potentially limit the transmission of drug-resistant viruses; and ZA/CG gel, a non-ARV microbicide.

*In vivo* animal studies have demonstrated promising proof-of-principle results for the ability of the MIV-150/ZA/CG and ZA/CG gels to significantly reduce immunodeficiency virus and HSV-2 infection when applied vaginally or rectally.

### PRODUCT DEVELOPMENT: RINGS

To expand prevention options for women and provide lasting protection, the Council is developing microbicide vaginal rings that protect against HIV and other STIs and can remain in place for one to three months. Because the ring is convenient and discreet and can stay in place for extended periods, women may be more likely to use it consistently, which would help ensure effectiveness.

Recent animal studies by the Council provided the first data indicating that an anti-HIV drug delivered in a vaginal ring is able to prevent vaginal immunodeficiency virus infection. These proof-of-concept studies have paved the way for the Council to develop vaginal rings carrying MIV-150 and zinc acetate—which is the most effective API combination for gels. The Council is developing rings made of silicone, polyurethane, or ethyl vinyl acetate (EVA)—all of which are physically stable, durable, and easy to distribute without requiring refrigeration.

### PRODUCT DEVELOPMENT: MULTIPURPOSE TECHNOLOGIES

The Council is developing multipurpose prevention technologies that combine antiviral and contraceptive

ingredients into one product for on-demand or long-term use. A dual-protection gel for women who have sex irregularly combines LNG, a contraceptive agent, with two antiviral agents (MIV-150 and zinc acetate). The Council is also developing this combination of drugs as an intravaginal ring for long-term use.

### FIELD RESEARCH: BEHAVIORAL AND METHODOLOGICAL STUDIES

Behavioral research is an integral part of the Council's comprehensive approach to microbicides development. Our research aims to increase adherence to product use, improve reporting of adherence and other sensitive behaviors that have an impact on study outcomes, identify more effective methods for recruiting the most appropriate study populations, and improve the informed consent process.

Several methodological experiments and technological developments are underway that: 1) improve our ability to validate self-reports from study participants about product use and sexual behavior with biomarkers and/or through multiple reporting methods; 2) examine the use of alternative recruitment strategies for enrolling trial participants who are highly motivated to follow the protocol and are representative of the women who might eventually use the product; and 3) collaborate with other organizations on the use of the Council's customized audio computer-assisted self-interview software in clinical trials.

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**The Population Council takes a broad and comprehensive approach to HIV prevention, care, and treatment.** In addition to basic research in immunology and development and introduction of a safe, effective microbicide, the Council conducts social science and health-related research to better understand the social and behavioral aspects of HIV and AIDS; and to develop, evaluate, and scale-up effective service-delivery models. For more information, visit [www.popcouncil.org/hivaids](http://www.popcouncil.org/hivaids).

For more information about the Population Council's work on microbicides, contact [pubinfo@popcouncil.org](mailto:pubinfo@popcouncil.org) or visit [www.popcouncil.org/microbicides](http://www.popcouncil.org/microbicides).

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The Population Council confronts critical health and development issues—from stopping the spread of HIV to improving reproductive health and ensuring that young people lead full and productive lives. Through biomedical, social science, and public health research in about 50 countries, the Council works with our partners to deliver solutions that lead to more effective policies, programs, and technologies to improve lives worldwide. Established in 1952 and headquartered in New York, the Council is a nongovernmental, nonprofit organization with an international board of trustees.