

# Microbicides Toolkit

Microbicides are substances that are being tested to help prevent the sexual transmission of HIV. Vaginal microbicides are intended as an HIV prevention option for women that, unlike male condoms, would not require negotiation with a partners. Rectal microbicides could be used by both men and women to reduce the risk of HIV infection during anal sex.

Most of the microbicides under study employ ARV drugs that are commonly used in pill form to treat an HIV infection. ARV pill formulations can also be used for HIV prevention in an approach called pre-exposure prophylaxis (PrEP). The World Health Organization recommends that PrEP be offered as a prevention option to HIV-negative people at substantial risk of HIV.

The toolkit provides information about microbicides and ARV-based HIV prevention for health policymakers, programs managers, community educators, trainers, advocates, and communication specialists. The toolkit can help readers prepare for the introduction of microbicides and develop implementation strategies once products come to the marketplace, The toolkit will be updated as the field progresses.

To find out whether a resource has already been included in this toolkit, visit the site map or type the title in the search box. Visit the About page for more detailed information about the selection of resources, a list of publishers, and other K4Health toolkits.

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**What are Toolkits?**

Toolkits are electronic collections of carefully selected information resources on a particular topic for health policy makers, program managers, and service providers. They were originally created under the Knowledge for Health (K4Health) Project. A selection of K4Health Toolkits have been carried forward to the Knowledge SUCCESS Project. The Toolkit platform is intended to make updating and adding resources simple for Toolkit managers, even if they do not have extensive skills in web content management.

### **What is the purpose of this toolkit?**

This toolkit contains resources to help advocates, policy makers, program managers, community educators, trainers, advocates, communication specialists, and other audiences prepare for the introduction of microbicides once an effective product becomes available.

### **Who developed this toolkit?**

FHI 360 developed this toolkit under the Knowledge for Health Project. The following individuals from other organizations also contributed their experience and expertise to review the toolkit and ensure its relevance and usefulness:

Quarraisha Abdool Karim, Centre for the AIDS Programme of Research in South Africa (CAPRISA)

Manju Chatani-Gada, AVAC

Mitzy Gafos, Medical Research Council Clinical Trials Unit

Lisa Levy, FHI 360/Microbicide Trials Network

Larry Miller, FHI 360

Jim Pickett, International Rectal Microbicide Advocates

Lisa Rossi, Microbicide Trials Network

Holly Seltzer, International Partnership for Microbicides

Kristine Torjesen, FHI 360 and the Microbicide Trials Network

Rhonda White, FHI 360 and the Microbicide Trials Network

Cynthia Woodsong, International Partnership for Microbicides

### **Who are the publishers of the resources?**

Resources selected for inclusion in this toolkit were published by organizations working throughout the world to develop microbicides and other HIV-prevention methods, including multipurpose technologies to prevent pregnancy and HIV or other sexually transmitted infections.

### **What types of resources are included?**

This toolkit is not a comprehensive library of all existing materials on microbicides. It provides essential background on microbicide research and development, key resources to support continued research, and practical information to guide future introduction of microbicides. These resources include:

- Up-to-date global and country-specific background and reference materials to inform advocacy and assist with the design of microbicide research and the eventual introduction of microbicides.
- Tools and guidelines for conducting ethical, effective and relevant research on microbicides and other biomedical methods of HIV prevention and for the introduction of new HIV-prevention methods.
- Publications that detail key processes and lessons learned from microbicide research and development.

### **Who are the intended audiences?**

Advocates and policymakers will find research and information to help them support microbicide research and plan for the introduction of effective products.

- Program managers will find background on microbicide research and other resources to help them prepare to introduce microbicides.
- Trainers and community educators will find tools and other resources for engaging community members in research that could be adapted to involve communities in microbicide introduction.
- Communication professionals can use the toolkit resources to explore strategies, methods, and messages to promote understanding of and support for microbicide research and facilitate introduction and scale-up of microbicide services.

### **How do I get started using this toolkit?**

To browse the content of this toolkit, use the navigation tabs above to view resources related to key topics. Each tab includes strategic resources, further organized by sub-topic. Click on the title of the resource for more information about it, or click on the full-text link to get direct access to the full resource. Some of the tools are readily available in an adaptable format (for example, Microsoft Word documents and PowerPoint presentations). We encourage you to alter and personalize these tools for your own use. (Please remember to credit the source).

### **Publishers of resources included in this toolkit**

Resources selected for inclusion in this toolkit were published by the following organizations that work throughout the world to develop, assess, advocate support for and prepare for introduction of microbicides and other HIV-prevention methods.

AIDSTAR-One

Alliance for Microbicide Development

AmFAR

AVAC

Centers for Disease Control and Prevention (CDC)

Centre for the AIDS Programme of Research in South Africa (CAPRISA)

Coalition Advancing Multipurpose Innovations (CAMI)

CONRAD

EngenderHealth

FHI 360

Gilead Sciences, Inc.

Global Campaign for Microbicides (GCM)

HIV/AIDS Network Coordination (HANC)

HIV Prevention Trials Network (HPTN)

HIV Vaccines and Microbicides Research Tracking Working Group

International AIDS Vaccine Alliance

International Partnership for Microbicides (IPM)

International Rectal Microbicides Advocates (IRMA)

Johns Hopkins Bloomberg School of Public Health

Joint United Nations Programme on HIV/AIDS (UNAIDS)

Kaiser Family Foundation

London School of Hygiene and Tropical Medicine

Microbicide Trials Network

Microbicides Development Programme

Microbicides Media and Communications Initiative

O'Neill Institute for National and Global Health Law, Georgetown University

PATH

The Population Council

Rockefeller Foundation Microbicide Initiative

The Wellcome Trust

Setshaba Research Centre

South African Medical Research Council

Southern African HIV Clinicians Society Consensus Committee

Starpharma

United Nations Development Programme

University of Cape Town

University of KwaZulu-Natal

University of North Carolina at Chapel Hill

U.S. Agency for International Development

U.S. Food and Drug Administration

U.S. National Institute of Allergy and Infectious Diseases

Wits Reproductive Health and HIV Institute

World Health Organization



## **Essential Knowledge**



The most widely studied microbicides were formulated as gels used either daily or before and after sex. Poor adherence to these study regimens heightened interest in long-acting microbicide candidates, such as a vaginal ring that slowly releases an antiretroviral drug over time.

In 2016, ASPIRE and The Ring Study, two trials of a vaginal ring containing the antiretroviral drug dapivirine, showed a modest protective effect against HIV, with greater efficacy among subgroups of participants with evidence of higher adherence. Follow-up studies suggest that women are willing to use the ring, which is being considered for licensure.

Additional vaginal and rectal microbicide candidates are moving through the research pipeline. Scientists believe that a microbicide that contains a combination of different active drugs will likely have the greatest impact on the HIV epidemic, and some vaginal products are being designed to prevent both HIV infection and unwanted pregnancies.

This section of the toolkit provides essential background and reference materials on the different types of microbicides, the need for effective products for women and men, the status of microbicide research, and how microbicides fit into the larger field of HIV prevention.

## **The Basics**

### **The Need**

### **Status of Microbicide Research**

### **Future of Microbicides**

### **Useful Links**

# **The Basics**

What are microbicides, and why are they needed? Could they be used by men and women? And when will they be available? The resources in this section provide basic information about microbicides in the context of biomedical HIV prevention, including information about topical and oral use of antiretroviral (ARV) drugs for HIV prevention.

Proof of concept has been demonstrated for both a vaginal microbicide containing an ARV drug and

for oral use of ARVs as pre-exposure prophylaxis (PrEP). The U.S. Food and Drug Administration and other drug regulatory agencies have approved a combination of the ARV drugs emtricitabine and tenofovir disoproxil fumarate (TDF/FTC, or Truvada) for daily use as oral PrEP to reduce the risk of HIV infection in uninfected men and women who are at high risk of HIV infection through sexual intercourse. Studies have also shown that early treatment of HIV-infected individuals with oral ARV drugs can dramatically reduce the risk of transmission to an uninfected partner as well as lowering the risk of serious illness and death. In September 2015, the World Health Organization recommended that anyone living with HIV begin antiretroviral therapy as soon after diagnosis as possible and that PrEP be offered as an option to all people living in contexts or communities with an HIV incidence of 3 percent.

Research is under way to identify multipurpose prevention technologies that could prevent a combination of pregnancy and HIV or other sexually transmitted infections. For example, researchers are assessing microbicide gels, gel capsules, or films that could be used with barrier methods of contraception and combinations of antiretroviral drugs and contraceptives that could be delivered via vaginal rings or diaphragms to prevent both pregnancy and HIV.

## Overview

Resources:

- **Rectal Microbicides**

The reasons why rectal microbicides are needed, challenges to their development, and the results of clinical trials on their safety and acceptability are described in this fact sheet.

- **Microbicide Overview**

This document provides information on the potential of microbicides for HIV prevention, the next steps for the monthly dapivirine ring, and the research and development process.

- **Microbicides for HIV Prevention: an Introductory Factsheet**

This fact sheet explains what microbicides are and provides a brief overview of the state of microbicide research.

- **Microbicides and HIV Prevention Research: Glossary of**

# Terms

A guide for understanding common terms used in the field of HIV prevention research is provided in this 75-page glossary. It includes medical and scientific terms, drug names, descriptions of international health organizations supporting microbicide work, and statistical terms to help interpret clinical trial results.

## Antiretroviral-Based Prevention

Resources:

- **The Future of ARV-Based Prevention and More**

The pipeline of non-vaccine HIV prevention products includes oral pills, vaginal rings, vaginal and rectal gels, vaginal films, long-acting injectable antiretrovirals, and more. Also pictured in this infographic are the range of multipurpose prevention technologies in development that aim to reduce the risk of HIV and sexually transmitted infections and/or provide effective contraception for women.

- **MTN-003 - VOICE**

Links to press statements, fact sheets, and other information about the VOICE (Vaginal and Oral Interventions to Control the Epidemic) trial conducted by the Microbicide Trials Network are provided on this page. VOICE evaluated the safety and effectiveness of three antiretroviral-based approaches for preventing sexual transmission of HIV in women: applying tenofovir gel daily or taking an antiretroviral tablet (tenofovir or Truvada) once a day. None of these approaches proved to be effective among the 5,029 women enrolled in the trial. The results showed that most of the participants did not use the study products daily as directed.

- **PrEPWatch**

The PrEPWatch website is a clearinghouse for information on pre-exposure prophylaxis for HIV prevention.

- **WHO Implementation Tool for Pre-exposure Prophylaxis (PrEP) of HIV Infection: Summary**

This summary document provides an overview of the WHO implementation tool for pre-exposure

prophylaxis (PrEP) of HIV infection, which is designed to support the implementation of PrEP among a range of populations in different settings.

- **WHO Implementation Tool for Pre-exposure Prophylaxis (PrEP) of HIV Infection**

The World Health Organization developed this series of 11 modules to support the implementation of PrEP among a range of populations in different settings. It addresses a need expressed by country partners for practical advice on how to consider the introduction of PrEP and begin its implementation.

- **Pre-Exposure Prophylaxis: An Introductory Factsheet**

Part of a series on emerging HIV prevention strategies, this document defines pre-exposure prophylaxis (PrEP), reviews the scientific evidence, and outlines key research, regulatory, and advocacy issues.

- **Introduction to Long-Acting Injectables**

This infographic details the process for developing long-acting injectables for pre-exposure prophylaxis and treatment.

- **Treatment as Prevention: An Introductory Factsheet**

"Treatment as prevention? is the use of combination antiretroviral therapy (ART) in HIV-positive individuals to preserve their health and reduce the risk of transmitting the virus. This fact sheet defines treatment as prevention, reviews the science behind it, and outlines priorities for advocating for its implementation.

- **Oral Pre-Exposure Prophylaxis: Questions and Answers**

An 11-page document from UNAIDS, WHO, and AVAC answers questions about oral pre-exposure prophylaxis (PrEP), addressing issues including safety, eligibility, potential risk compensation, implementation, and cost-effectiveness.

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# Ongoing and Planned PrEP Demonstration and Implementation Studies

This summary table of ongoing and planned global PrEP evaluation studies can be downloaded in Excel.

- **HPTN 083 Summary**

The HIV Prevention Trials Network (HPTN) is conducting a Phase 2b/3 double-blind safety and efficacy study of injectable cabotegravir compared to daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for pre-exposure prophylaxis among HIV-uninfected cisgender men and transgender women who have sex with men.

- **FEM-PrEP**

A webpage provides a description of the FEM-PrEP trial of pre-exposure prophylaxis for HIV prevention among women and links to fact sheets and publications describing the results of the trial and related research.

## Multipurpose Prevention Technologies

Resources:

- **The Future of ARV-Based Prevention and More**

The pipeline of non-vaccine HIV prevention products includes oral pills, vaginal rings, vaginal and rectal gels, vaginal films, long-acting injectable antiretrovirals, and more. Also pictured in this infographic are the range of multipurpose prevention technologies in development that aim to reduce the risk of HIV and sexually transmitted infections and/or provide effective contraception for women.

- **A Multipurpose Prevention Ring for Women's Sexual and Reproductive Health**

This fact sheet addresses the need for multipurpose prevention technologies and describes an MPT that the International Partnership for Microbicides is testing, a vaginal ring that contains the antiretroviral drug dapivirine and the contraceptive hormone levonorgestrel.

- **MPTs for Reproductive Health**

Multipurpose prevention technologies (MPTs) are defined and described in this fact sheet, which also explains how these technologies could save lives by combining family planning and prevention of sexually transmitted infections, including HIV.

- **Status of Modelling Efforts in the Field of Multipurpose Prevention Technologies: Summary Report**

The Initiative for Multipurpose Prevention reports on the findings of a review of modeling studies of the health impact and cost-effectiveness of multipurpose prevention technologies (MPTs). This summary report also addresses gaps in the research and next steps.

- **Multipurpose Prevention Technologies: An Introductory Factsheet**

Women around the world face dual risks of HIV infection and unintended pregnancy. This fact sheet describes the need for multipurpose prevention technologies (MPT) and presents the MPT products in the development pipeline.

- **Multipurpose Prevention Technologies for the Developing World: U.S. Investment is Critical**

Published in the *Guttmacher Policy Review* in the summer of 2015, this article makes the case for greater investment in the development of multipurpose prevention technologies (MPTs) that would provide protection against multiple health risks, such as unintended pregnancy, HIV, and sexually transmitted infections. No large pharmaceutical company has a significant program in MPT research, so the development of these promising products depends on support from governments and foundations.

- **Assessing the Potential of MPTs in South Africa, Uganda**

## and Nigeria

Market research conducted by Ipsos with support from the Bill & Melinda Gates Foundations assessed the acceptability of multipurpose prevention technologies (MPTs) among women in South Africa, Uganda, and Nigeria, focusing on four potential MPTs: injectables, implants, intravaginal film, and intravaginal rings. This webpage provides links to a booklet about the study, regional maps, and a summary of the quantitative results and their implications.

- ### Global Reproductive Health Diaries

Global Reproductive Health Diaries presents the stories of real women in India, Ivory Coast, China, the USA, and Guatemala, illustrating the need for multipurpose prevention technologies.

- ### Developing Multipurpose Reproductive Health Technologies: An Integrated Strategy

Published in the journal AIDS Research and Treatment, this paper reviews an innovative and iterative strategy for developing multipurpose reproductive health technologies ? products designed explicitly to simultaneously address the need for both contraception and protection from sexually transmitted infections, including HIV infection.

- ### MPT Product Development Database

This searchable database, maintained by the Initiative for Multipurpose Prevention Technologies (IMPT), includes the MPT products that are currently available or in active development.

## The Need

Vaginal microbicides will give more power to women who have trouble negotiating condom use with their partners or who otherwise need a prevention option that can be used discreetly. Because the risk of HIV infection is up to 20 times higher during unprotected anal intercourse than during unprotected vaginal intercourse, rectal microbicides will be an important prevention option both for women who engage in anal intercourse and for men who have sex with men.

Resources:

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# **Microbicides: Women-Centered HIV Prevention Products to Help End AIDS by 2030**

The International Partnership for Microbicides explains why microbicide research and development is a smart investment for women's health, economic growth, and gender equality.

- ## **Why Microbicides for Women?**

The International Partnership for Microbicides explains why women urgently need a method they can use to protect themselves from HIV infection and describes the essential role microbicides could play in a comprehensive HIV prevention strategy.

- ## **MPTs for Reproductive Health**

Multipurpose prevention technologies (MPTs) are defined and described in this fact sheet, which also explains how these technologies could save lives by combining family planning and prevention of sexually transmitted infections, including HIV.

- ## **Dapivirine Ring: The Case for Action**

This report examines the need for the the dapivirine monthly ring, its potential contribution to HIV prevention, and the steps that must be taken while the product is clearing initial regulatory approvals to ensure speedy access for women and girls.

- ## **Family Planning Evidence Brief: Expanding Contraceptive Choice**

This brief report, prepared by the World Health Organization for the 2017 Family Planning Summit, highlights evidence to support the expansion of contraceptive options for women, including multipurpose technologies.

- ## **Video: Microbicides ? Developing New HIV Prevention Options for Women**

A monthly vaginal ring that releases a drug for HIV prevention has been shown to safely help reduce the risk of infection and could give women a novel way to protect themselves. This video describes the latest research and the next steps for the dapivirine ring.

- **The Rectal Revolution is Here - Video and Facilitator's Guide**

?The Rectal Revolution is Here: An Introduction to Rectal Microbicide Clinical Trials,? is designed to educate communities affected by HIV about the development of rectal microbicides and the importance of participating in clinical trials to speed the search for new HIV prevention methods. Produced by Paw Print Productions of Cape Town, South Africa, the video is available for viewing on YouTube in English, Spanish, and Thai. A facilitator's guide is also available in English, Spanish, and Thai.

- **Infographic: Why is Women's Sexual and Reproductive Health Integral to Global Development?**

This infographic depicts how HIV prevention for women supports global development goals in health, poverty reduction, education, and gender equality.

## **Status of Microbicide Research**

AVAC regularly updates its HIV Prevention Research and Development Database with information about planned, ongoing, and past trials of biomedical methods of HIV prevention. Users can search by prevention option (microbicides) and status (ongoing) to learn about current trials of microbicide candidates. See the Clinical Research section of this toolkit for additional information on the clinical research process, current microbicide trials, and results of past trials.

Resources:

- **HIV Prevention Research and Development Database**

This searchable database, originally developed and maintained by the Alliance for Microbicide Development, has been expanded to provide a comprehensive source of information about planned, ongoing, and completed clinical trials of biomedical HIV prevention methods.

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# MPT Product Development Database

The searchable MPT Product Development Database includes multipurpose technology products that are currently available, as well as MPT products in active development.

## Future of Microbicides

Planning, implementation research, and preparations for regulatory approval and manufacturing are essential now to avoid delays in bringing microbicides to market once effective products have been identified. Strategy and planning documents and reports on efforts to prepare for microbicide introduction can be found in this section.

Resources:

- **HIV Prevention Research and Development Database**

This searchable database, originally developed and maintained by the Alliance for Microbicide Development, has been expanded to provide a comprehensive source of information about planned, ongoing, and completed clinical trials of biomedical HIV prevention methods.

- **The Promise of the Ring for Women's HIV Prevention**

Watch this video to learn about the dapivirine vaginal ring and the International Partnership for Microbicides' next steps to potentially put the product into the hands of women at high risk of HIV.

- **IPM Clinical Trials**

This regularly updated resource includes a list of all the International Partnership for Microbicides' ongoing and planned trials of dapivirine in the form of a ring, a tablet, and a ring combining dapivirine with maraviroc, another antiretroviral drug.

- **MPT Product Development Database**

The searchable MPT Product Development Database includes multipurpose technology products that are currently available, as well as MPT products in active development.

## Useful Links

More information about microbicide research and development, advocacy, and preparations for introduction is available on the following websites:

Alliance for Microbicide Development

AmFAR

AVAC

Centers for Disease Control and Prevention (CDC)

Centre for the AIDS Programme of Research in South Africa (CAPRISA)

ClinicalTrials.gov

CONRAD

EngenderHealth

Follow-on African Consortium for Tenofovir Studies (FACTS)

FEM-PrEP

FHI 360

Gilead Sciences, Inc.

Global Campaign for Microbicides

HIV/AIDS Network Coordination (HANC)

HIV Prevention Trials Network

HIV Vaccines and Microbicides Research Tracking Working Group

Initiative for Multipurpose Prevention Technologies

International AIDS Vaccine Initiative

International Partnership for Microbicides (IPM)

International Rectal Microbicides Advocates (IRMA)  
Johns Hopkins Bloomberg School of Public Health  
Joint United Nations Programme on HIV/AIDS (UNAIDS)  
Kaiser Family Foundation  
London School of Hygiene and Tropical Medicine  
Medical Research Council  
Microbicide Trials Network  
Microbicide Product Introduction Initiative  
PATH  
Setshaba Research Centre  
South African Medical Research Council  
Starpharma  
The Population Council  
United Nations Development Programme  
University of Cape Town  
University of KwaZulu-Natal  
University of North Carolina at Chapel Hill  
U.S. Agency for International Development  
U.S. Food and Drug Administration  
U.S. National Institute of Allergy and Infectious Diseases  
Wellcome Trust  
Wits Reproductive Health and HIV Institute (RHI)  
World Health Organization

# Clinical Research

In 2016, a vaginal ring containing the antiretroviral drug dapivirine became the first microbicide product to be shown effective against HIV in two clinical trials. In those trials, known as ASPIRE and The Ring Study, rates of HIV protection were higher among women older than 21, who tended to use the rings more consistently. Two open-label extension studies of the monthly dapivirine ring also yielded promising results, and the International Partnership for Microbicides is pursuing global and national regulatory approval to license the product in countries where women face the highest risk of acquiring HIV.

Other clinical trials continue to explore the safety and effectiveness of various vaginal and rectal microbicide candidates. This section contains resource materials that highlight recent clinical research on microbicides.

The design and conduct of a single microbicide clinical trial is a sophisticated undertaking that may involve several countries, dozens of scientists and staff members, and thousands of research participants. Readers will find resources that can help them understand the scope and complexity of these trials, including information on ethical considerations, participant safety, community engagement, potential drug resistance, and HIV prevention and care for study participants.

## Clinical Research Results

Several microbicide candidates have been ruled out through large-scale effectiveness trials that have helped guide the field of microbicide research toward more promising products. Two trials have shown that a vaginal ring containing the antiretroviral drug dapivirine is safe to use and reduces women's risk of HIV acquisition. Trials of other potential microbicides, including a rectal formulation of tenofovir gel, are ongoing.

Resources with information about all completed effectiveness (Phase IIb and Phase III) trials of microbicide candidates are listed on the study product pages. Additional products that are being evaluated are described on the Current and Planned Trials page of the toolkit. For another up-to-date summary of microbicide effectiveness trials and their results, see AVAC's HIV Prevention Research and Development Database.

## Dapivirine ring

Resources:

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## **ASPIRE ? MTN 020**

Links are provided to information about ASPIRE (A Study to Prevent Infection with a Ring for Extended Use), a Phase III safety and effectiveness trial of a vaginal ring containing the antiretroviral drug dapivirine that enrolled 2,629 women at several sites in Africa and was one of two trials of this monthly ring to demonstrate a protective effect against HIV infection. This page also provides links to information about follow-up studies, including HOPE (HIV Open-Label Prevention Extension), and efforts to seek regulatory approval based on the results of ASPIRE and its "sister" study, the Ring Study.

- ### **The Ring Study**

This page on the website of the International Partnership for Microbicides (IPM) provides information and links to resources about The Ring Study, a clinical trial designed to determine whether a monthly vaginal ring that delivers the antiretroviral drug dapivirine helps prevent HIV infection in women and is safe for long-term use. The Ring Study, which enrolled 1,959 women at six sites in South Africa and one site in Uganda, was one of two trials of the dapivirine ring to demonstrate a protective effect against HIV. Links to information about related studies and IPM's dapivirine ring licensure program are also provided.

- ### **After The Ring Study: DREAM**

A fact sheet about DREAM (Dapivirine Ring Extended Access and Monitoring), an open-label extension study that provided monthly dapivirine rings for one year to women who had participated in The Ring Study, provides information on the purpose, design, and results of the study.

- ### **REACH HIV Prevention Study in Africa (Video)**

Aimed at potential study participants, this video provides background and describes the purpose and design of the Reversing the Epidemic in Africa with Choices in HIV prevention (REACH) study, or MTN-034. REACH is an open-label trial to evaluate how adolescent girls and young women use the monthly dapivirine vaginal ring and oral Truvada® (FTC/TDF) as daily pre-exposure prophylaxis (PrEP).

- ### **Use of a Vaginal Ring Containing Dapivirine for HIV-1**

## **Prevention in Women**

Published in the New England Journal of Medicine on December 1, 2016, this article reports on the results of A Study to Prevent Infection with a Ring for Extended Use (ASPIRE). The authors conclude that a monthly vaginal ring containing dapivirine reduced the risk of HIV-1 infection among African women, with increased efficacy among subgroups of the study population with evidence of more consistent use of the ring.

- ### **ASPIRE and The Ring Study Results ? A Snapshot**

The results of two randomized clinical trials of the use of a dapivirine vaginal ring for HIV prevention, A Study to Prevent Infection with a Ring for Extended Use (ASPIRE) and The Ring Study, are summarized in a table.

- ### **Safety and Efficacy of a Dapivirine Vaginal Ring for HIV Prevention in Women**

The results of The Ring Study, a randomized controlled trial that evaluated the safety and efficacy of extended use of a vaginal ring containing dapivirine for the prevention of HIV infection among women in South Africa and Uganda, were published December 1, 2016, in The New England Journal of Medicine. The authors concluded that the dapivirine ring was not associated with any safety concerns and was associated with a rate of acquisition of HIV-1 infection that was lower than the rate with placebo.

- ### **Sister Studies: The Ring Study and ASPIRE**

The Ring Study and ASPIRE (A Study to Prevent Infection with a Ring for Extended Use) are described in this fact sheet. The two related trials showed that monthly use of a vaginal ring that delivers the antiretroviral drug dapivirine can help prevent HIV infection in women and is safe for long-term use.

- ### **Video: Microbicides ? Developing New HIV Prevention Options for Women**

A monthly vaginal ring that releases a drug for HIV prevention has been shown to safely help reduce the risk of infection and could give women a novel way to protect themselves. This video

describes the latest research and the next steps for the dapivirine ring.

- **MTN025 ? HOPE**

Links are provided to information about the results and background of the HIV Open Label Prevention (HOPE) trial, a follow-on to the ASPIRE trial in which former ASPIRE participants were offered the opportunity to use the dapivirine ring in the context of a study. MTN conducted this trial to gather additional information on the ring's safety, how women use the ring knowing that it can help reduce their risk of HIV, and the relationship between adherence and HIV protection.

- **REACH Study (MTN034)**

Links are provided to information about Reversing the Epidemic in Africa with Choices in HIV prevention (REACH), or MTN-034, a trial evaluating how adolescent girls and young women use the monthly dapivirine vaginal ring and oral Truvada® (FTC/TDF) as daily pre-exposure prophylaxis (PrEP). The Microbicide Trials Network is conducting this trial to gain a better understanding of the HIV prevention needs and preferences of adolescent girls and young women and to collect information on the safety of both approaches for women in these age groups.

- **IPM Clinical Trials**

This regularly updated resource includes a list of all the International Partnership for Microbicides' ongoing and planned trials of dapivirine in the form of a ring, a tablet, and a ring combining dapivirine with maraviroc, another antiretroviral drug.

## Tenofovir gel

Resources:

- **MTN-003 - VOICE**

Links to press statements, fact sheets, and other information about the VOICE (Vaginal and Oral Interventions to Control the Epidemic) trial conducted by the Microbicide Trials Network are provided on this page. VOICE evaluated the safety and effectiveness of three antiretroviral-based approaches for preventing sexual transmission of HIV in women: applying tenofovir gel daily or taking an antiretroviral tablet (tenofovir or Truvada) once a day. None of these approaches proved

to be effective among the 5,029 women enrolled in the trial. The results showed that most of the participants did not use the study products daily as directed.

- **Tenofovir 1% Vaginal Gel for Prevention of HIV-1 Infection in Women in South Africa (FACTS-001): a Phase 3, Randomised, Double-Blind, Placebo-Controlled Trial**

The primary results of FACTS 001, a randomized, placebo-controlled trial conducted in South Africa to evaluate the safety and efficacy of 1% tenofovir vaginal gel, are presented in an article in *The Lancet Infectious Diseases*.

- **Vaginal Bacteria Modify HIV Tenofovir Microbicide Efficacy in African Women (Abstract)**

This study, published in the journal *Science*, provides evidence linking vaginal bacteria to microbicide efficacy through tenofovir depletion via bacterial metabolism.

- **HIV Prevention Study Does Not Confirm Tenofovir Gel Effectiveness**

Tenofovir vaginal gel was not effective in preventing HIV among a large, diverse population of young South African women, reports this press release from the Follow-on African Consortium for Tenofovir Studies. Less than a quarter of the participants were able to use the gel consistently. The press release discusses the results presented at the 2015 Conference on Retroviruses and Opportunistic Infections and their implications.

- **FACTS 001 Trial: Questions and Answers**

Questions and answers about the FACTS 001 efficacy trial of the use of tenofovir vaginal gel among women in South Africa provide background on the study and information about its results and their implications.

- **MTN Statement on Decision to Discontinue Use of Tenofovir Gel in VOICE, a Major HIV Prevention Study in Women**

This press release discusses the decision to discontinue the tenofovir vaginal gel group in the VOICE (Vaginal and Oral Interventions to Control the Epidemic) HIV prevention trial. The decision came after a November 2011 routine review of study data collected from September 9, 2009, through September 30, 2011, concluded that tenofovir gel was safe but not effective in preventing HIV in the women enrolled in the trial. Further analysis of the data, released March 4, 2013, with the results of the VOICE trial, suggests that most of the women did not use the gel daily: tenofovir was detected in the blood samples of one-quarter of the study participants.

- **AIDS 2010: July 20, 2010: Results of the CAPRISA 004 Trial**

Dr. Salim Abdool Karim of CAPRISA announces the results of the CAPRISA 004 trial in this 70-minute video. The results, which showed proof-of-concept for microbicides, were presented in the International AIDS Conference 2010 session "Safety and Effectiveness of 1% Tenofovir Vaginal Microbicide Gel in South African Women: Results of the CAPRISA 004 Trial." A link for accessing a transcript of the session is provided.

- **CAPRISA 004 Tenofovir Gel Trial**

This web page provides an overview of the CAPRISA 004 trial, including a summary of key results and implications for future research. Links to a study background, fact sheets, and other resources are also provided.

- **Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women**

The full scientific article, published in the journal *Science*, is available for the CAPRISA 004 trial. This double-blind, randomized controlled trial demonstrated that tenofovir gel used before and after sex reduced HIV acquisition by an estimated 39 percent among women in the trial, and by 54 percent among the women with high gel adherence.

- **Gabi's Gift (CAPRISA 004 Video)**

This five-minute video follows one woman from the beginning of her participation in the CAPRISA 004 study of tenofovir gel to her joy when hearing the results.

# Tenofovir gel (formulated for rectal use)

Resources:

- **Rectal Microbicides**

The reasons why rectal microbicides are needed, challenges to their development, and the results of clinical trials on their safety and acceptability are described in this fact sheet.

- **MTN-017**

Links are provided to information about MTN-017. The first Phase II trial of a rectal microbicide, MTN-017 found that a reduced-glycerin formulation of tenofovir gel was safe when used daily and before and after sex. Study participants were just as likely to follow through using an anti-HIV gel with anal sex as they were to using daily oral pre-exposure prophylaxis (PrEP).

- **MTN-017: A Rectal Phase 2 Extended Safety and Acceptability Study of Tenofovir Reduced-Glycerin 1% Gel**

The results of a Phase II trial of reduced-glycerin 1% tenofovir gel among men who have sex with men and transgender women, published in *Clinical Infectious Diseases*, found that rectal application of the gel was safe and acceptable. Adherence and reported likelihood of future use were similar for intermittent use of the gel and a daily oral PrEP regimen, but lower for the daily gel regimen.

## Current and Planned Trials

For the most up-to-date summaries of all current trials, see AVAC's HIV Prevention Research and Development Database, and Px Wire, a quarterly update on biomedical HIV prevention research. Additional information is available from the International Partnership for Microbicides about current IPM Clinical Trials and from the Microbicide Trials Network about Ongoing, Planned and Completed Trials of the MTN.

Resources:

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## IPM Clinical Trials

This regularly updated resource includes a list of all the International Partnership for Microbicides' ongoing and planned trials of dapivirine in the form of a ring, a tablet, and a ring combining dapivirine with maraviroc, another antiretroviral drug.

## Research Process

A potential microbicide candidate is first assessed in laboratory studies and animal models. If it passes this stage of testing, it enters human clinical trials. In Phase I trials, scientists assess the safety of the product, determine its acceptability, and identify its appropriate dose and formulation. In Phase II trials, scientists again assess safety and acceptability, but among more participants and for a longer period. The final stages of microbicide trials (Phase IIb and Phase III trials) are used to collect information about a product's long-term safety and evaluate its effectiveness in preventing HIV. These trials often enroll thousands of participants who live in communities where the risk of HIV infection is very high.

This section of the toolkit highlights several important issues that must be considered as clinical trials are designed and conducted. A high standard of research ethics, engagement of community members and other research stakeholders, and various measures for maintaining the safety of the research participants are all essential. Procedures also need to be in place to help participants adhere to the proper use of the study product and make sure they receive the best possible care for the prevention and treatment of HIV.

Resources:

- **HIV Prevention Trials Terms: An Advocates Guide**

This fact sheet explains some of the terms used to talk about trials designed to test new HIV prevention tools.

- **A Toolkit for Developing Bilingual Lexicons for International HIV Prevention Clinical Trials**

Researchers often use technical terminology that trial participants may not easily understand. Those working on international clinical trials face additional communication challenges when local languages do not have scientific or technical vocabularies in relevant subject areas. This toolkit

guides researchers through a process for identifying or improving translations of clinical research terms that are difficult to translate or comprehend.

- **AVAC Fact Sheet: Data Safety Monitoring Boards**

This fact sheet helps advocates learn more about how clinical trials are monitored and regulated by a variety of entities, including independent bodies that review the trial protocol and data on an ongoing basis to ensure that the trial is ethical and should continue. Some situations in which a data safety monitoring board has made a recommendation that affected the conduct of a trial are reviewed.

- **When Do You Stop an HIV Prevention Trial for Futility? A Primer for HIV Prevention Advocates**

This fact sheet examines why trials are stopped early for ?futility,? explaining the meaning of this term in the context of a clinical trial, when such a recommendation is made, and how it might affect other trials.

- **Advocates' Guide to Statistical Terms**

AVAC's fact sheet explains some of the main statistical terms used to describe the results of clinical trials, including statistical significance, confidence interval, and intent-to-treat analysis.

## **Research Ethics**

The basic principles of respect, beneficence, and justice guide the development and conduct of all research involving human participants. Within this framework, the informed consent process helps ensure that all who volunteer for a study understand the potential benefits and risks of the study and are able to make an informed choice about whether to participate. Research ethics also affect the communities in which research is conducted, as community members frequently have input into the development, design, and implementation of clinical trials.

Resources:

- **Bill of Rights and Responsibilities for HIV Research**

This document, developed for clinical trial networks supported by the Division of AIDS of the U.S. National Institutes of Health, provides a short list of the rights and responsibilities of participants in a clinical trial. The purpose of this document is to help research participants act on their own behalf and in partnership with study staff.

- **Respect, Protect, Fulfill: Best Practice Guidance in Conducting HIV Prevention Research with Gay, Bisexual and Other Men Who Have Sex with Men (MSM) in Rights-Constrained Environments**

This guidance offers practical advice on how to engage men who have sex with men in research trials of promising HIV prevention and treatment interventions, including HIV vaccines, rectal microbicides, combinations of prevention methods, and pre-exposure prophylaxis. The guidance aims to maximize the benefits and minimize the risks to men who have sex with men, communities, and researchers.

- **Ethical Considerations in Biomedical HIV Prevention Trials**

Updated in 2012, this document offers guidance on ethical considerations in HIV prevention research based on extensive consultation and lessons learned in biomedical HIV prevention research. Although the guidelines specifically address trials of biomedical HIV preventive interventions, they are also relevant to trials of behavioral HIV prevention methods.

- **Principles of Research Ethics**

The three principles of ethical research ? respect for persons, beneficence, and justice ? are explained in this fact sheet.

- **Research Ethics in Action**

This webpage describes various approaches to putting into practice laws and guidelines on the ethical conduct of research. The approaches include informed consent, ethics committee reviews, and aspects of study design.

- **Ethical Guidance Document**

AVAC compiled this listing of key guidelines and laws on the ethical conduct of research, with a brief summary of each document and its contribution to the field of biomedical research. Some are historical documents, and others are periodically updated. The year reported in this list represents the first year the document was published.

## Community Engagement

Microbicide researchers strive to engage community members early in the research process to help ensure that a clinical trial will meet local needs and ethical standards at all levels. Involving the community in the development, design, and implementation of a clinical trial also gives community members ownership of the research process and facilitates their potential use of the product or intervention under study. Establishing a community advisory board, typically composed of community members who can represent the views and experiences of the study population, is one of the most common mechanisms for engaging communities in clinical research.

Resources:

- **Stakeholder Engagement Toolkit for HIV Prevention Trials**

The *Stakeholder Engagement Toolkit for HIV Prevention Trials* is a guide to engaging a wide range of key stakeholders ? people living with HIV, communities, policymakers, advocates, governments, religious and cultural leaders, funders, international agencies and regulatory bodies ? at every stage of a clinical trial from planning to implementation and sharing results. A *Toolkit Quick Guide*, added in 2014 based on feedback from people working in community outreach in research settings, gives users quick and easy access to modifiable (Microsoft Word or Excel) tools and instructions for using them. Resources to support face-to-face group training events are also provided.

- **Respect, Protect, Fulfill: Best Practice Guidance in Conducting HIV Prevention Research with Gay, Bisexual and Other Men Who Have Sex with Men (MSM) in Rights-Constrained Environments**

This guidance offers practical advice on how to engage men who have sex with men in research trials of promising HIV prevention and treatment interventions, including HIV vaccines, rectal microbicides, combinations of prevention methods, and pre-exposure prophylaxis. The guidance aims to maximize the benefits and minimize the risks to men who have sex with men,

communities, and researchers.

- **Recommendations for Community Involvement in National Institute of Allergy and Infectious Diseases HIV/AIDS Clinical Trials Research**

This document is the product of extensive community experience and expertise from around the world, providing a tool for researchers and community representatives to further expand and deepen existing partnerships and forge new ones in HIV/AIDS clinical trials research. Links to the English and Spanish versions are included.

- **Good Participatory Practice Tools**

Developed to help research teams and other stakeholders understand, implement, and monitor the Good Participatory Practice Guidelines, these resources include templates, checklists, and training tools, as well as a link to a four-month online training course about the guidelines.

- **Good Participatory Practice: Guidelines for Biomedical HIV Prevention Trials. Second edition.**

This 88-page document outlines good participatory practice (GPP) guidelines and systematic guidance on how trial funders, sponsors, and implementers can effectively engage with all stakeholders in the design and conduct of biomedical HIV prevention trials. The GPP guidelines are divided into three main sections: the importance of and need for GPP in biomedical HIV prevention trials, guiding principles of GPP, and optimal GPP practices for biomedical HIV prevention trials.

- **Community Partners Training Materials**

Materials for educating community advisory board members about the clinical research process and their role in it include PowerPoint slides and instructor notes, a participant guide, workshop activities, handouts, and an instructor's guide.

## **Safety**

Many safeguards are in place to keep study participants safe during clinical trials. Because the earliest trials of new microbicide candidates specifically evaluate safety, only the safest products and the safest amounts of those products are used in later trials. Side effects and other possible adverse events are closely monitored and recorded during the trials, and independent groups known as data and safety monitoring boards are assembled to regularly review the safety data and make important decisions about trial continuation.

Resources:

- **AVAC Fact Sheet: Data Safety Monitoring Boards**

This fact sheet helps advocates learn more about how clinical trials are monitored and regulated by a variety of entities, including independent bodies that review the trial protocol and data on an ongoing basis to ensure that the trial is ethical and should continue. Some situations in which a data safety monitoring board has made a recommendation that affected the conduct of a trial are reviewed.

## Adherence

In the context of a clinical trial, adherence refers to the extent to which study participants use the assigned study products or follow study regimens as directed. It can be measured through self-reports, through direct observation, or by using a variety of more objective measures. Adherence data are important for accurately assessing the safety and effectiveness of the study products. Data on why participants did or did not adhere to a study regimen are also useful for designing future clinical trials and for adjusting current trials to improve adherence levels. These data will also be needed to optimize adherence levels once an effective microbicide product is introduced into the market.

Resources:

- **An Interdisciplinary Framework for Measuring and Supporting Adherence in HIV Prevention Trials of ARV-Based Vaginal Rings**

Correct, consistent use of study products and measurement of adherence to study regimens have emerged as critical challenges in the evaluation of HIV prevention technologies. This article, published in a September 2014 supplement to the Journal of the International AIDS Society, presents an interdisciplinary framework for systematically investigating promising strategies to support product uptake and adherence and to measure adherence in randomized, blinded clinical

trials of antiretroviral-based vaginal rings.

- **Perspectives on Use of Oral and Vaginal Antiretrovirals for HIV Prevention: the VOICE-C Qualitative Study in Johannesburg, South Africa**

The VOICE trial of tenofovir-based vaginal gel and pills was unable to demonstrate efficacy for HIV prevention because of low adherence to study regimens. This study, published in a September 2014 supplement to the *Journal of the International AIDS Society*, explores views of and experiences with the use of antiretrovirals for HIV prevention among VOICE participants, their male partners, and community members and examines the implications for adherence.

- **Adherence Support Approaches in Biomedical HIV Prevention Trials: Experiences, Insights and Future Directions from Four Multisite Prevention Trials**

Published in the journal *Culture and Behavior*, this paper provides a synthesis of the adherence support experiences from four pivotal PrEP trials ? the Centre for the AIDS Programme of Research in South Africa (CAPRISA) 004, FEM-PrEP, Iniciativa Prophylaxis (iPrEx), and Vaginal and Oral Interventions to Control the Epidemic (VOICE).

- **Long-term Consistent Use of a Vaginal Microbicide Gel among HIV-1 Sero-discordant Couples in a Phase III Clinical Trial (MDP 301) in Rural South-west Uganda**

This article, published in the 1 February 2013 issue of the online journal *Trials*, reports on an assessment of the factors associated with consistent gel use in the MDP 301 clinical trial to assess the microbicide candidate PRO 2000 among HIV-negative women in serodiscordant couples in southwestern Uganda. The study found that women 25 years or older and those living in a household with three or more rooms for sleeping compared with one room were more likely to report consistent use of the gel.

- **Microbicide Clinical Trial Adherence: Insights for Introduction**

Drawing primarily from data and experience from large-scale microbicide efficacy trials, this article published in the Journal of the International AIDS Society identifies lessons learned about adherence to study regimens in six areas: 1) adherence measurement in clinical trials, 2) comprehension of use instructions/instructions for use, 3) unknown efficacy and its effect on adherence/messages regarding effectiveness, 4) partner influence on use, 5) retention and continuation, and 6) the generalizability of trial participants' adherence behavior. For each topic, recommendations are provided for using trial findings to prepare for future microbicide trials, post-marketing research, and microbicide introduction and delivery programs.

- **Adherence in HIV Prevention Research: A Primer for HIV Prevention Advocates**

This two-page fact sheet provides basic information on what adherence is and why it is important in HIV prevention trials. It also describes how adherence is measured in microbicide trials and discusses the advantages and limitations of each method.

- **Adherence and Its Measurement in Phase 2/3 Microbicide Trials**

The authors of this 12-page substantive review, published in the journal AIDS and Behavior, observe that optimizing and measuring adherence to study regimens have emerged as critical challenges for clinical trials of topical microbicides. Drawing on data-driven presentations from several focused meetings, this article synthesizes lessons from past microbicide trials and provides recommendations for future trials of microbicides and other HIV prevention technologies.

- **Assessing the Accuracy of Adherence and Sexual Behaviour Data in the MDP301 Microbicides Trial Using a Mixed Methods and Triangulation Model**

The Microbicides Development Programme has developed a mixed-method/triangulation model for generating more accurate data on adherence and sexual behavior in microbicide and other HIV-related research. The authors of this nine-page article conclude that integrating in-depth interviews and triangulation into clinical trials could increase the richness and accuracy of behavioral and adherence data.

- **FEM-PrEP Adherence Publications**

This page provides links to articles or article abstracts from the FEM-PrEP trial of the effectiveness of pre-exposure prophylaxis for HIV prevention among women at high risk of acquiring HIV infection. It includes a section on articles about adherence to daily PrEP among the trial participants.

## Drug Resistance

Viruses and other harmful organisms can become resistant to the drugs that are used to prevent or treat them. This can happen for a variety of reasons, including the use of suboptimal levels of a drug or the use of a drug when it is not needed. Microbicide researchers minimize the risk that HIV will become resistant to a particular microbicide by making sure that women who are infected with HIV do not use the study drug and that those who become infected with HIV during a trial discontinue use.

Resources:

- **Questions and Answers: HIV Drug Resistance and ARV-Based Prevention**

Twenty-five questions and answers about HIV drug resistance and antiretroviral-based prevention are divided into two broad categories 1) the basics of drug resistance and 2) drug resistance and HIV prevention in this five-page document. Additional information about HIV drug resistance and ARV-based prevention can be found at: <http://www.mtnstopshiv.org/news/studies/mtn003>.

- **Understanding HIV Drug Resistance in the Context of Microbicides and Pre-Exposure Prophylaxis (PrEP)**

This clear and accessible two-page fact sheet explains the basic concept of HIV drug resistance and how it occurs by posing and answering four key questions. The document includes simple, illustrative diagrams and a summary of important points to remember.

## Standards of HIV Prevention and Care

Microbicide researchers are committed to providing a high standard of HIV prevention and care to all study participants. Participants are provided with counseling, condoms, and sometimes additional services to help them prevent HIV infection during a trial. Researchers also make agreements with

local hospitals and other health facilities to ensure that participants who become infected with HIV during the trial will receive appropriate health care. Men and women who are found to be HIV-positive during screening are also referred to high-quality affordable services to meet their physical and psychological needs.

Resources:

- **HIV Research in the Era of PrEP: The Implications of TDF/FTC for Biomedical Prevention Trials**

Recommendations on the provision of pre-exposure prophylaxis (PrEP) in HIV prevention trials, based on a review of the scientific literature and a survey of community-based advocates (including members of the advisory boards of such trials), are summarised in this white paper.

- **Research Ethics in Action**

This webpage describes various approaches to putting into practice laws and guidelines on the ethical conduct of research. The approaches include informed consent, ethics committee reviews, and aspects of study design.

## **Implementation Research**

Implementation research seeks to bridge the potential gap between the efficacy of a microbicide during a clinical trial and its effectiveness in the real world.

Bridging that gap requires a thorough understanding of the factors that might affect a product's effectiveness. How will a new microbicide be integrated into local health services? Will the microbicide be accepted by the general public, and how will knowing that a product works affect acceptance and adherence? What is the most cost-effective way to provide the microbicide? Will drug resistance become an issue after long-term use of the microbicide? Such questions are the subject of implementation research to expedite and sustain access to proven products.

### **Preparing for Introduction**

#### **Acceptability and Affordability**

#### **Impact and Cost-effectiveness**

#### **Access and Delivery**

Resources:

- **After The Ring Study: DREAM**

A follow-on to The Ring Study of a dapivirine ring, the Dapivirine Ring Extended Access and Monitoring (DREAM) open-label extension study is providing the active ring to former Ring Study participants ? and young women using the ring for the first time ? while the product is under regulatory review for licensure.

- **HOPE and Beyond: Next Steps and Planned Studies of the Dapivirine Vaginal Ring**

The HIV Open-Label Extension (HOPE) study offers former participants in the ASPIRE study of the dapivirine vaginal ring the opportunity to use the ring in the context of a study while researchers collect additional data on safety and adherence. This Q&A document provides information about HOPE and other studies of the dapivirine ring, including REACH, which will evaluate how adolescent girls and young women use the monthly ring and daily oral pre-exposure prophylaxis.

- **Rolling Out Tenofovir Gel in Family Planning Clinics: The CAPRISA 008 Implementation Trial (Abstract)**

CAPRISA 008 was a two-arm, open-label, randomized controlled, non-inferiority implementation trial that provided participants from CAPRISA 004 with post-trial access to tenofovir gel while generating evidence that could be used for future implementation of topical pre-exposure prophylaxis (PrEP) among women. Its findings on the delivery of a microbicide containing tenofovir gel in family planning clinics are reported in this chapter of a book about HIV prevention and treatment trials conducted by the Centre for the AIDS Programme of Research in South Africa.

- **PrEPWatch: Implementation Initiatives**

A special section of PrEPWatch ? an online clearinghouse of information about pre-exposure prophylaxis (PrEP) against HIV ? provides updates on the implementation of PrEP. This section includes descriptions of donor initiatives to expand access to PrEP, which include links to resources and information about PrEP introduction in specific countries.

# Preparing for Introduction

Researchers are identifying the regulatory processes and requirements for the licensure of a microbicide in different countries and are exploring how to optimize access (advocacy and local manufacture) and promote use of microbicides once they are available. They are also considering the implications of introductory activities on women and girls and are modeling the contribution that microbicides could make to HIV prevention efforts.

Resources:

- **The Dapivirine Ring Design Guide: Human-Centered Design Research to Increase Uptake and Use**

This guide provides an overview of design concepts to promote sustained use of the dapivirine ring and describes how the concepts were developed through a human-centered design approach. The guide also provides a link to a supplementary library of online resources, such as editable templates and supporting visuals, that can be used to adapt selected concepts.

- **Dapivirine Ring: The Case for Action**

This report examines the need for the the dapivirine monthly ring, its potential contribution to HIV prevention, and the steps that must be taken while the product is clearing initial regulatory approvals to ensure speedy access for women and girls.

- **Plan 4 PrEP: Toolkit for Oral PrEP Implementation**

A set of tools is available to support national planning for rollout and scale-up of oral pre-exposure prophylaxis. These tools are based on the experience of the Optimizing Prevention Technology Introduction on Schedule (OPTIONS) Consortium, which supported ministries of health and technical working groups in South Africa, Kenya, and Zimbabwe to develop strategies for introducing oral PrEP.

- **Setting the Stage for ARV-Based Prevention for Women: A Snapshot of the Zimbabwean Context**

A program brief summarizes the findings of a landscape analysis conducted in Zimbabwe as part of a process developed by the Population Council to help policymakers and program managers identify the most strategic opportunities for introducing tenofovir gel. Based on a desk review and interviews with key decision makers, the brief reviews the epidemiologic context of the HIV epidemic, highlights policies and programs related to HIV, and provides other information relevant to potential introduction of tenofovir vaginal gel in Zimbabwe.

- **Policy And Programme Considerations For ARV-Based Prevention For Women: Insights From Key Opinion Leaders In Zimbabwe About Tenofovir Gel**

This report describes the process and outcomes of a systematic inquiry among key opinion leaders in Zimbabwe about program and policy considerations to address in preparation for the potential introduction of tenofovir gel. Most respondents were supportive of introducing tenofovir gel should it prove effective, with several caveats, and safety and efficacy were the chief concerns of all respondents.

- **Tenofovir Gel for HIV Prevention for Women: Perspectives of Key Opinion Leaders from India**

This abstract of an article published in *Health Policy and Technology* presents key opinion leaders' perspectives from India on the introduction of tenofovir vaginal gel for HIV prevention among women. Overall, respondents were supportive but expressed caveats about the role tenofovir gel might play in the overall HIV-prevention program.

- **Communicating about Microbicides with Women in Mind: Communication Strategy and Adaptation Guide**

This final report for the Communicating about Microbicides with Women in Mind project was written to: 1) document the promise of vaginal microbicide gel as a new HIV prevention product for women, 2) describe the project's experience with materials development, 3) provide a sample microbicide communication strategy for Kenya, and 4) outline a process for updating and adapting the materials for use in other countries or with other new HIV prevention methods. Copies of the materials, including English- and Swahili-language materials and other project documents, are shown in an annex to the report.

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## **Communicating About Microbicides with Women in Mind (fact sheet)**

The Communicating about Microbicides with Women in Mind project developed a two-page document highlighting the project's major accomplishments, including details about the three project phases conducted in Kenya: 1) landscape analysis, 2) materials development and pretesting, and 3) materials assessment and key results.

- ### **Manual for Conducting a Gender Analysis for Microbicide Introduction**

This manual provides guidance for conducting a gender analysis in a country preparing to introduce microbicides. A gender analysis can strengthen the effectiveness of health and development programming by identifying gender inequalities that may affect program outcomes and potential ways to address those inequalities. The manual outlines the steps to conducting a gender analysis for microbicide introduction, shares lessons learned from pilot testing in Kenya and South Africa, and provides tools and resources for conducting a gender analysis for microbicide introduction.

- ### **A Pocket Guide to Thinking about Gender & Vaginal Microbicides in South Africa**

FHI 360 and Sonke Gender Justice conducted a gender analysis in South Africa to identify gender-related barriers and opportunities to women's microbicide access and use and to make recommendations for addressing those barriers. This pocket card, created with input from the South African National AIDS Council (SANAC) Men's and Women's sectors, is designed to build support for a gender-integrated microbicides rollout among community members and policy makers.

- ### **Program and Policy Considerations for Tenofovir Gel in India**

A program brief summarizes the findings of a landscape analysis conducted in India as part of a process developed by the Population Council to help policymakers and program managers identify the most strategic opportunities for introducing tenofovir gel. Based on a desk review and interviews with key decision makers, the brief reviews the epidemiologic context of the HIV epidemic, highlights policies and programs related to HIV, and provides other information relevant to potential introduction of tenofovir vaginal gel in India.

- **Shaping the Operations Research Agenda for Antiretroviral-Based Prevention Products for Women: Gels and Rings**

In 2012 the Population Council organized a consultation on an operations research agenda as part of a larger initiative, funded by the US Agency for International Development, to prepare for microbicide introduction. The consultation report outlines the ideas the 40 participants generated for priority research topics and approaches.

## **Acceptability and Affordability**

The needs and perceptions of women are crucial for the effective implementation of a microbicide product. Would a woman prefer using a gel or a ring? Or would she prefer other HIV prevention approaches, such as oral pre-exposure prophylaxis? Additional research is needed to determine the best ways to deliver these products to the women who need them most, without stigmatizing their use. Research is also needed to determine the best ways to involve men in supporting microbicide use, while protecting women's ability to decide whether to use them and to discuss the decision with their male partners.

Microbicides will not be acceptable if they cost too much. A microbicide's cost to a user will be influenced by the manufacturing costs, so research organizations and sponsors are exploring options for local manufacture to reduce those costs. Financing will be an important part of this equation.

Resources:

- **A Review of Social and Behavioral Factors Influencing Dapivirine Ring Use**

The purpose of this literature review is to provide a comprehensive overview of social and behavioral findings from dapivirine ring studies, to inform an investment case for the dapivirine ring and guide further research to prepare for uptake. Most completed studies addressed

acceptability and adherence, but the review also examines factors such as partner buy-in, product preferences, and ring delivery. A bibliography is available at: <http://www.prepwatch.org/mpii-tools-resources/>.

- **Social Context of Adherence in an Open-Label 1% Tenofovir Gel Trial: Gender Dynamics and Disclosure in KwaZulu-Natal, South Africa**

CAPRISA 008, an open-label extension study of tenofovir vaginal gel with coitally related dosing, provided an opportunity to explore the relationship between product adherence and gender dynamics in a context where women knew they were receiving an active product with evidence of HIV prevention effectiveness. Interviews with 63 study participants and 13 male partners in KwaZulu-Natal, South Africa, highlighted that the process of negotiating gel use was determined in part by relationship dynamics.

- **Engaging Male Partners in Women's Microbicide Use: Evidence and Recommendations**

Vaginal microbicides are considered a groundbreaking HIV prevention tool because women can initiate their use, but male partners have played an important role in product acceptability and adherence to study regimens in clinical trials. This document synthesizes the evidence on men's roles in women's use of microbicides in clinical trials and makes recommendations for engaging male partners in future microbicide research and product introduction.

- **Preparing for Rectal Microbicides: Sociocultural Factors Affecting Product Uptake Among Potential South American Users**

Published in the June 2014 issue of the American Journal of Public Health, this article reports on the results of a qualitative study conducted among 140 men who have sex with men and transgender women in Lima and Iquitos, Peru, and Guayaquil, Ecuador, to explore their views on rectal microbicides and identify factors that could affect uptake of a rectal microbicide.

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# Assessing the Potential of MPTs in South Africa, Uganda and Nigeria

Market research conducted by Ipsos with support from the Bill & Melinda Gates Foundations assessed the acceptability of multipurpose prevention technologies (MPTs) among women in South Africa, Uganda, and Nigeria, focusing on four potential MPTs: injectables, implants, intravaginal film, and intravaginal rings. This webpage provides links to a booklet about the study, regional maps, and a summary of the quantitative results and their implications.

- ## Acceptability of Vaginal Film, Soft-gel Capsule, and Tablet as Potential Microbicide Delivery Methods among African Women (abstract)

A total of 526 sexually active women ages 18 to 30 years participated in a consumer product preference study in Burkina Faso, Tanzania, and Zambia. The women were asked to use each of three products (placebo formulations of a vaginal tablet, film, and soft-gel capsule) once daily for seven consecutive days for a total of 21 days. Data suggest that the availability of microbicides in multiple dosage forms may increase acceptability and adherence and, therefore, effectiveness. This abstract summarizes an eight-page paper published in the *Journal of Women's Health*.

- ## PAS I: Gel Product Attribute Study

This page on the International Partnership for Microbicides website describes the study design and summarizes the results of a study conducted among 543 women at seven locations in Kenya, South Africa, and Zambia to assess whether vaginal gels will be acceptable to, and used by, women in Africa. A link to the final report on the study is provided.

- ## PAS II: Vaginal Gel, Tablet and Soft Capsule Preferences

This page on the International Partnership for Microbicides website describes the design of a study that assessed and compared placebo vaginal tablets, films, and soft gel capsules (without active ingredient) in several urban and semi-urban areas of Burkina Faso, Tanzania, and Zambia. The results were published in the *Journal of Women's Health*. A link is provided to the abstract.

- ## Sexual Communication among Married Couples in the

## Context of a Microbicide Clinical Trial and Acceptability Study in Pune, India

The results of a study exploring couple-level sexual communication and socio-cultural norms that influence couples' communication about sex are reported in this 14-page paper, which was published in the journal *Culture, Health & Sexuality*. The findings suggest that creating safe spaces for couples where they can ask frank questions about HIV and AIDS, sex, and sexuality could improve couples' communication about sex and reduce their risk of HIV infection.

- **Acceptability and Adherence of a Candidate Microbicide Gel among High-Risk Women in African and India**

A 15-page paper, published in *Culture, Health & Sexuality*, examines qualitative, in-depth post-trial interview data from a Phase III clinical trial of cellulose sulfate microbicide gel in two sites in Africa (Uganda and Benin) and two in India (Chennai and Bagalkot) to better understand the factors that influence microbicide acceptability and adherence in a clinical trial setting.

- **Intravaginal Insertion in KwaZulu-Natal: Sexual Practices and Preferences in the Context of Microbicide Gel Use**

Published in *Culture, Health & Sexuality*, this 13-page paper uses qualitative data from women in a Microbicides Development Programme clinical trial as well as from women and men in the community where the trial was conducted to examine whether the use of intravaginal insertions conflicts with the introduction of microbicide gels in a rural part of KwaZulu-Natal, South Africa. This is the first study to make this comparison, and the findings provide evidence that vaginal microbicide gels may be more acceptable in communities where intravaginal insertion is practiced than was previously thought.

## Impact and Cost-effectiveness

Models encompassing various scenarios have produced encouraging results: millions of HIV infections could be averted and the incidence of HIV significantly decreased through the introduction of microbicides or oral pre-exposure prophylaxis. Modeling studies will be needed to assess the potential contributions of these methods to combinations of HIV prevention methods in different settings.

Resources:

- **Dapivirine Ring Modeling Literature Review**

The aim of this literature review is to identify the scope of completed dapivirine ring and microbicide modeling to date, to inform modeling work that the OPTIONS Consortium intends to undertake in 2017. A bibliography is available at: <http://www.prepwatch.org/mpii-tools-resources/>.

- **Status of Modelling Efforts in the Field of Multipurpose Prevention Technologies: Summary Report**

The Initiative for Multipurpose Prevention reports on the findings of a review of modeling studies of the health impact and cost-effectiveness of multipurpose prevention technologies (MPTs). This summary report also addresses gaps in the research and next steps.

- **Cost-effectiveness of Tenofovir Gel in Urban South Africa: Model Projections of HIV Impact and Threshold Product Prices**

Published in *BMJ Infectious Diseases*, this article reports on a modeling study that used the results of the CAPRISA 004 trial of tenofovir gel to estimate the population-level impact of the gel on HIV and HSV-2 transmission and the price thresholds at which widespread product introduction would be as cost-effective as male circumcision for HIV prevention in urban South Africa.

## **Access and Delivery**

Who will have access to microbicides? How will that decision be made? Access and delivery plans must consider the needs of women, address the potential barriers to access, and provide guidance to providers and to women.

Resources:

- **IPM?s Application for Dapivirine Vaginal Ring for Reducing**

## **HIV Risk in Women Now Under Review by European Medicines Agency**

In a July 13, 2017 press release, the International Partnership for Microbicides (IPM) announces that its application for the monthly dapivirine vaginal ring is under review by the European Medicines Agency (EMA). The release also outlines plans to submit applications to other regulatory authorities in pursuit of licensure.

- ### **A Review of Social and Behavioral Factors Influencing Dapivirine Ring Use**

The purpose of this literature review is to provide a comprehensive overview of social and behavioral findings from dapivirine ring studies, to inform an investment case for the dapivirine ring and guide further research to prepare for uptake. Most completed studies addressed acceptability and adherence, but the review also examines factors such as partner buy-in, product preferences, and ring delivery. A bibliography is available at: <http://www.prepwatch.org/mpii-tools-resources/>.

- ### **Rolling Out Tenofovir Gel in Family Planning Clinics: The CAPRISA 008 Implementation Trial (Abstract)**

CAPRISA 008 was a two-arm, open-label, randomized controlled, non-inferiority implementation trial that provided participants from CAPRISA 004 with post-trial access to tenofovir gel while generating evidence that could be used for future implementation of topical pre-exposure prophylaxis (PrEP) among women. Its findings on the delivery of a microbicide containing tenofovir gel in family planning clinics are reported in this chapter of a book about HIV prevention and treatment trials conducted by the Centre for the AIDS Programme of Research in South Africa.

- ### **Guidance for Providing Informed-Choice Counseling on Sexual Health for Women Interested in Pre-Exposure Prophylaxis (PrEP)**

This guide offers clear, step-by-step guidance on counseling women who are interested in using pre-exposure prophylaxis (PrEP) to help them make informed choices about their sexual health. Based on the informed-choice counseling traditionally used in family planning, the guide helps counselors acknowledge and support many different approaches to HIV risk reduction while

encouraging women to consider how these approaches apply to their individual needs and circumstances.

- **Oral Pre-Exposure Prophylaxis: Putting a New Choice in Context**

Produced collaboratively by UNAIDS, WHO, and AVAC, this publication is intended to complement WHO's recommendations on pre-exposure prophylaxis (PrEP) and support the optimal use of oral PrEP to protect individuals and contribute to ending the AIDS epidemic.

- **Microbicides Readiness Assessment Tool**

FHI 360 designed this tool to help managers in public health facilities evaluate the extent to which a facility has the material, technical, and human resources necessary to provide microbicides. The tool is a product of a mixed-methods study that examined the implementation of Kenya's Minimum Package for Reproductive Health ? HIV Integrated Services in public-sector health centers from March 2013 to August 2014.

- **Preparing for the Delivery of Microbicides: Lessons from the Implementation of Integrated Reproductive Health and HIV Services**

This brief summarizes the results of a mixed methods study in Kenya that measured the extent to which integrated services are delivered to targeted beneficiaries in public-sector health facilities as intended and identified the health systems-level factors that facilitate and impede effective delivery of integrated reproductive health and HIV services.

- **HIV Prevention for Women in Kenya: An Advocacy Guide for Gender-Sensitive Microbicide Introduction**

Based on findings from a gender analysis in Kenya, these advocacy tools can be used to raise awareness of key gender issues that need to be addressed in planning for microbicide introduction in Kenya. The guide includes: (1) a summary of gender issues that will affect women's microbicide access and use; (2) guidance for policymakers and program designers on developing a gender-transformative microbicide introduction program; and (3) three case studies that nongovernmental organizations and other advocates in the community can use to generate discussion about microbicides.

- **Findings from a Gender Analysis for Microbicide Introduction in South Africa**

FHI 360 and Sonke Gender Justice conducted a gender analysis for microbicide introduction in South Africa. The process included a desk review, interviews with key stakeholders, and an interpretation meeting to identify gender norms and inequalities that increase women's HIV risk and could inhibit women's access and adherence to microbicides in the future. This brief outlines 11 strategies that could be part of a microbicide introduction program to overcome these gender-related barriers.

- **Assessing Physical Delivery of PrEP in Support of Proof of Deliverability: Results from Kenya**

The findings from an assessment of the feasibility and potential impact of delivering antiretroviral (ARV)-based oral and injectable pre-exposure prophylaxis (PrEP) and vaginal microbicide gels in Kenya are summarized in this brief. Conducted from December 1, 2010, to December 31, 2012, the study was designed to: 1) identify the most feasible and acceptable channels for delivery of ARV-based prevention products to populations at high risk of HIV infection; 2) evaluate the potential impact of such delivery on existing health services; and 3) identify the additional capacity required to support product introduction.

- **Assessing Physical Delivery of PrEP in Support of Proof of Deliverability: Results from South Africa**

The findings from an assessment of the feasibility and potential impact of delivering antiretroviral (ARV)-based oral and injectable pre-exposure prophylaxis (PrEP) and vaginal microbicide gels in South Africa are summarized in this brief. Conducted from December 1, 2010, to December 31, 2012, the study was designed to: 1) identify the most feasible and acceptable channels for delivery of ARV-based prevention products (oral and injectable pre-exposure prophylaxis, or PrEP, and vaginal microbicide gels) to populations at high risk of HIV infection; 2) evaluate the

potential impact of such delivery on existing health services; and 3) identify the additional capacity required to support product introduction.

- **CAPRISA 008**

This webpage describes a follow-up study to the CAPRISA 004 tenofovir gel trial, CAPRISA 008, which assessed the feasibility and effectiveness of distributing tenofovir gel through family planning clinics in communities where the CAPRISA 004 trial took place.

## Policy and Guidelines



The implementation of a microbicide strategy will require

guidance and coordination from normative bodies, such as the World Health Organization and the Joint United Nations Programme on HIV/AIDS, as well as consultations with governments and other stakeholders. Each microbicide will need approval from national regulatory agencies, such as the Food and Drug Administration in the United States or the Medicines Control Council in South Africa, wherever the strategy will be implemented. All of these efforts must be coordinated with national policies and strategies on the introduction of new HIV prevention technologies.

### Key Resources

### Guidelines

## Key Resources

Resources:

- **IPM?s Application for Dapivirine Vaginal Ring for Reducing**

## **HIV Risk in Women Now Under Review by European Medicines Agency**

In a July 13, 2017 press release, the International Partnership for Microbicides (IPM) announces that its application for the monthly dapivirine vaginal ring is under review by the European Medicines Agency (EMA). The release also outlines plans to submit applications to other regulatory authorities in pursuit of licensure.

- ## **Day of Dialogue on Multipurpose Prevention Technologies: Toward Clarity in Nomenclature**

A 2011 meeting drew together nearly 30 stakeholders to discuss specific opportunities and challenges for the regulatory pathway for multipurpose prevention technologies. The meeting also helped the Population Council chart next steps to facilitate regulatory approval for multipurpose prevention technologies for sexual and reproductive health.

- ## **Facilitating Regulatory Approval of Multipurpose Prevention Technologies for Sexual and Reproductive Health**

This two-page document outlines the response of the U.S. Agency for International Development to an unmet need for products that provide simultaneous protection against unintended pregnancy and sexually transmitted infections, including HIV, with specific focus on the Population Council's work toward facilitating regulatory approval for multipurpose prevention technologies.

## **Guidelines**

Resources:

- ## **Southern African Guidelines for the Safe Use of Pre-Exposure Prophylaxis in Persons at Risk of Acquiring HIV-1 Infection**

In March 2016 the Southern African HIV Clinicians Society updated its first guidelines on pre-exposure prophylaxis (PrEP), advising that PrEP is a highly effective, safe, biomedical option for HIV prevention that can be incorporated with other combination prevention strategies in Southern Africa, given the high prevalence of HIV in the region. These guidelines explain what PrEP is, provide indications for its use in countries in southern Africa, outline steps for appropriate client selection, and offer guidance for monitoring and maintaining clients on PrEP.

- **Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection. Recommendations for a Public Health Approach ? Second edition**

The World Health Organization (WHO) provides guidance on the diagnosis of HIV infection, the use of antiretroviral drugs for treating and preventing HIV infection, and the care of people living with HIV in this update of its 2013 consolidated guidelines on the use of antiretroviral drugs. WHO produced this second edition following an extensive review of the evidence and consultations with experts and other stakeholders in mid-2015.

- **Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: What's New - Policy Brief**

Published in advance of the second edition of the World Health Organization's consolidated guidelines on the use of antiretrovirals (WHO, 2016) this policy brief summarizes the 10 recommendations in the updated guidelines and highlights what is new, based on an extensive review of the evidence conducted in 2015.

- **Consolidated Guidelines on HIV Prevention, Diagnosis, Treatment and Care for Key Populations**

For the first time, the World Health Organization brings together guidelines for HIV prevention, diagnosis, treatment, and care for key populations in one document. These consolidated guidelines provide a comprehensive package of evidence-related recommendations on HIV services for men who have sex with men, people who inject drugs, people in prisons and other closed settings, sex workers, and transgender people.

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# Truvada for a Pre-exposure Prophylaxis Indication

Gilead Sciences, Inc., the manufacturer of Truvada, provides information and links to resources on its safe use for pre-exposure prophylaxis for health care providers, HIV-negative individuals, and educators on this web page.

## Advocacy and Communication



Communication is integral to advocacy to promote and

support ethical, relevant research on microbicides and, eventually, access to proven products for those who need them most. Communication also plays a key role in in other aspects of microbicide development and implementation. This section includes resources for advocates and other communicators.

**Advocacy**

**Communication**

## Advocacy

Advocates work with community leaders, civil society groups, policymakers, program managers, and other constituencies to ensure that local stakeholders have a voice in the design and conduct of microbicide research and to encourage support for research and development. Advocacy will continue to be important to ensure that plans for introducing microbicides respond to the needs of these stakeholders and particularly to the needs of potential microbicide users. Advocates can work with governments, funders, manufacturers, and others to expedite access to microbicides for those who need them most and to do so in ways that empower, rather than stigmatize, microbicide users. This section provides resources for advocates, including reports, fact sheets, films, and toolkits.

## Reports

Resources:

- **Dapivirine Ring: The Case for Action**

This report examines the need for the the dapivirine monthly ring, its potential contribution to HIV prevention, and the steps that must be taken while the product is clearing initial regulatory approvals to ensure speedy access for women and girls.

- **HIV Prevention Research & Development Investments, 2000-16: Investment Priorities to Fund Innovation in a Challenging Global Health Landscape**

This annual accounting of funding for biomedical HIV prevention research tracks trends and identifies gaps in investment. In 2016, funding for HIV prevention R&D decreased by US\$35 million from the previous year to a total of US\$1.17 billion ? the lowest recorded annual investment in more than a decade. A link to the full archive of past resource tracking reports is provided.

- **2014-15 AVAC Report: Prevention on the Line**

AVAC?s report for 2014-15 puts the discussion about global targets for ending the AIDS epidemic in context. It discusses what makes a good target, explains why certain targets have worked in the past, and analyzes the state of HIV prevention targets and plans as of February 2015. The online version of the report includes links to graphics, videos, and a slide deck.

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## **Data Watch: Closing a Persistent Gap in the AIDS Response**

In *Data Watch: Closing a Persistent Gap in the AIDS Response*, AVAC and amFAR take stock of global progress toward ending the AIDS epidemic and lay out an agenda for improving accountability through better data collection. This document is an update to An Action Agenda to End AIDS, which includes clear, time-bound targets for outcomes, as well as the responsibilities of different stakeholders to achieve these targets.

- ### **On the Map: Ensuring Africa's Place in Rectal Microbicide Research and Advocacy**

This is a 29-page report on a strategy development meeting, hosted by International Rectal Microbicide Advocates in December 2011 in Addis Ababa, Ethiopia. The meeting brought together African stakeholders and allies representing a wide array of perspectives, experiences, and regions to develop action steps for an African rectal microbicide research and advocacy agenda. The group prioritized seven key action areas.

- ### **GLAM Toolkit: Advocacy to Improve Access to Safe, Condom-Compatible Lubricant, Version 2.0**

The Global Lube Access Mobilization (GLAM) developed this toolkit to propose concrete strategies for increasing access to lubricants in Africa. The toolkit offers tools and ideas to help civil society and government partners secure affordable, sustainable supplies of condom-compatible lubricants.

## **Fact Sheets**

Resources:

- ### **Why Microbicides for Women?**

The International Partnership for Microbicides explains why women urgently need a method they can use to protect themselves from HIV infection and describes the essential role microbicides could play in a comprehensive HIV prevention strategy.

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## **MPTs for Reproductive Health**

Multipurpose prevention technologies (MPTs) are defined and described in this fact sheet, which also explains how these technologies could save lives by combining family planning and prevention of sexually transmitted infections, including HIV.

- ### **HIV Prevention on the Line: Executive Summary**

Published in advance of the full version of AVAC's report for 2014-15, this four-page document summarises the state of HIV prevention research and implementation and the targets, strategies, and resources needed to end the AIDS epidemic.

- ### **Safety of Lubricants for Rectal Use: Questions and Answers for HIV Educators and Advocates**

This fact sheet assesses the current state of the science on the safety of lubricants for rectal use. It also summarizes the activities of a working group of researchers and advocates convened in early 2009 to discuss the testing of sexual lubricants for rectal safety and lists ongoing advocacy efforts.

## **Films**

Resources:

- ### **Video: Microbicides ? Developing New HIV Prevention Options for Women**

A monthly vaginal ring that releases a drug for HIV prevention has been shown to safely help reduce the risk of infection and could give women a novel way to protect themselves. This video describes the latest research and the next steps for the dapivirine ring.

- ### **The Promise of the Ring for Women?s HIV Prevention**

Watch this video to learn about the dapivirine vaginal ring and the International Partnership for Microbicides's next steps to potentially put the product into the hands of women at high risk of HIV.

- **The Rectal Revolution is Here - Video and Facilitator's Guide**

The Rectal Revolution is Here: An Introduction to Rectal Microbicide Clinical Trials, is designed to educate communities affected by HIV about the development of rectal microbicides and the importance of participating in clinical trials to speed the search for new HIV prevention methods. Produced by Paw Print Productions of Cape Town, South Africa, the video is available for viewing on YouTube in English, Spanish, and Thai. A facilitator's guide is also available in English, Spanish, and Thai.

- **Gabi's Gift (CAPRISA 004 Video)**

This five-minute video follows one woman from the beginning of her participation in the CAPRISA 004 study of tenofovir gel to her joy when hearing the results.

## Toolkits

Resources:

- **Stakeholder Engagement Toolkit for HIV Prevention Trials**

The *Stakeholder Engagement Toolkit for HIV Prevention Trials* is a guide to engaging a wide range of key stakeholders – people living with HIV, communities, policymakers, advocates, governments, religious and cultural leaders, funders, international agencies and regulatory bodies – at every stage of a clinical trial from planning to implementation and sharing results. A *Toolkit Quick Guide*, added in 2014 based on feedback from people working in community outreach in research settings, gives users quick and easy access to modifiable (Microsoft Word or Excel) tools and instructions for using them. Resources to support face-to-face group training events are also provided.

- **HIV Prevention for Women in Kenya: An Advocacy Guide for Gender-Sensitive Microbicide Introduction**

Based on findings from a gender analysis in Kenya, these advocacy tools can be used to raise awareness of key gender issues that need to be addressed in planning for microbicide introduction in Kenya. The guide includes: (1) a summary of gender issues that will affect women's microbicide access and use; (2) guidance for policymakers and program designers on developing a gender-transformative microbicide introduction program; and (3) three case studies that nongovernmental organizations and other advocates in the community can use to generate discussion about microbicides.

- **Global Lube Access Mobilization Toolkit**

Analyses among different populations in various settings indicate that oil-based products are the most common form of lubrication used for anal and vaginal sex, but oil-based lubricants significantly reduce the effectiveness of condoms. The Global Lube Access Mobilization project developed this toolkit to offer tools and ideas to aid African civil society and government partners in securing affordable condom-compatible lubricants. The toolkit includes a fact sheet, case studies, the results from a survey and review of African national strategic plans on HIV/AIDS, and a list of possible advocacy activities.

## **Additional Resources**

Resources:

- **HIV Prevention Trials Terms: An Advocates Guide**

This fact sheet explains some of the terms used to talk about trials designed to test new HIV prevention tools.

- **Global Reproductive Health Diaries**

Global Reproductive Health Diaries presents the stories of real women in India, Ivory Coast, China, the USA, and Guatemala, illustrating the need for multipurpose prevention technologies.

- **When Do You Stop an HIV Prevention Trial for Fertility? A Primer for HIV Prevention Advocates**

This fact sheet examines why trials are stopped early for ?futility,? explaining the meaning of this term in the context of a clinical trial, when such a recommendation is made, and how it might affect other trials.

- **Ten Steps to Organising a Community Forum on Microbicides**

Beginning with identifying the benefits of a well-organized community forum, this document provides clear, step-by-step directions for organizing a successful forum on microbicides.

## **Communication**

Clear and frequent communication is essential to ensure that study participants and communities are true partners in microbicide research. Effective messages are needed to explain the purpose of a study, the research process, and the results and their implications. And communication to a variety of audiences ? including potential users, health care providers, men, policymakers, and the media ? will be a critical part of microbicide introduction. Communication campaigns will be needed to generate demand for new products, promote adherence to microbicide regimens, convey the importance of routine HIV testing, emphasize the continued need for risk reduction through safe behavior, and create a supportive environment for microbicide use.

Resources:

- **The Dapivirine Ring Design Guide: Human-Centered Design Research to Increase Uptake and Use**

This guide provides an overview of design concepts to promote sustained use of the dapivirine ring and describes how the concepts were developed through a human-centered design approach. The guide also provides a link to a supplementary library of online resources, such as editable templates and supporting visuals, that can be used to adapt selected concepts.

- **Guidance for Providing Informed-Choice Counseling on Sexual Health for Women Interested in Pre-Exposure Prophylaxis (PrEP)**

This guide offers clear, step-by-step guidance on counseling women who are interested in using pre-exposure prophylaxis (PrEP) to help them make informed choices about their sexual health. Based on the informed-choice counseling traditionally used in family planning, the guide helps counselors acknowledge and support many different approaches to HIV risk reduction while encouraging women to consider how these approaches apply to their individual needs and circumstances.

- **Communicating About Microbicides with Women in Mind (fact sheet)**

The Communicating about Microbicides with Women in Mind project developed a two-page document highlighting the project's major accomplishments, including details about the three project phases conducted in Kenya: 1) the landscape analysis, 2) the materials development and pretesting, and 3) the materials assessment and key results.

- **Communications Handbook for Clinical Trials: Strategies, Tips, and Tools to Manage Controversy, Convey Your Message, and Disseminate Results**

Using case studies and practical insights culled from communications experience in clinical trials from around the world, this handbook covers the spectrum of communications planning, strategies, and activities needed at each stage of a clinical trial. It offers practical guidance to clinical trial staff and research partners on how to anticipate and respond to the special communication challenges posed by the conduct of clinical research. First published in 2010, the handbook is now available online with additional resources, including videos, slide presentations and new case studies.

- **Communicating about Microbicides with Women in Mind: Prototype Materials**

The Communicating about Microbicides with Women in Mind project worked with Artful Eyes Productions, a local Kenyan creative agency, to develop a suite of evidence-based, prototype communication materials to support the introduction of vaginal microbicide gel in Kenya should a microbicide be proven effective. Specifically designed to promote vaginal gel use in Kenya, these materials will need to be adapted for use in other countries or for other HIV prevention products. They will also need to be updated to reflect any new clinical information or usage guidelines that are developed once a vaginal gel has been licensed for use.

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# **Communicating about Microbicides with Women in Mind: Communication Strategy and Adaptation Guide**

This final report for the Communicating about Microbicides with Women in Mind project was written to: 1) document the promise of vaginal microbicide gel as a new HIV prevention product for women, 2) describe the project's experience with materials development, 3) provide a sample microbicide communication strategy for Kenya and 4) outline a process for updating and adapting the materials for use in other countries or with other new HIV prevention methods. Copies of the materials, including English- and Swahili-language materials, and other project documents are shown in an annex to the report.

- **??One Teabag Is Better than Four??: Participants Response to the Discontinuation of 2% PRO2000/5 Microbicide Gel in KwaZulu-Natal, South Africa**

This eight-page paper reports on ethnographic, participant-observation research undertaken to systematically collect participant responses to the discontinuation of the evaluation of 2% PRO2000/5 gel during a large Phase III clinical trial. In-depth interviews and focus group discussions were conducted with participants discontinued from the 2% gel. A total of 72 field reports, 12 in-depth interviews, and three focus groups with 250 women were completed for this analysis.

- **Microbicide Messaging: Themes to Emphasize and Avoid**

In this fact sheet, the Global Campaign for Microbicides identifies and discusses seven key points to consider when developing presentations about microbicides.

## **Training**



A microbicide trial routinely provides training to

members of the local community and to members of a community advisory board ? often formed specifically for the trial ? as well as to other community groups. Interactive training sessions focus on research literacy, research ethics, and the potential use of microbicides for HIV prevention. The community is typically engaged before any participants have been recruited for the trial, as well as during the trial and the dissemination of results.

This page includes some of materials used to train community members and community advisory boards. It also includes materials that can guide investigators on how to engage the community and tools for introducing and building capacity in the use of good participatory practice guidelines.

Resources:

- **Communications Handbook for Clinical Trials: Strategies, Tips, and Tools to Manage Controversy, Convey Your Message, and Disseminate Results**

Using case studies and practical insights culled from communications experience in clinical trials from around the world, this handbook covers the spectrum of communications planning, strategies, and activities needed at each stage of a clinical trial. It offers practical guidance to clinical trial staff and research partners on how to anticipate and respond to the special communication challenges posed by the conduct of clinical research. First published in 2010, the handbook is now available online with additional resources, including videos, slide presentations and new case studies.

- **Good Participatory Practice Tools**

Developed to help research teams and other stakeholders understand, implement, and monitor the Good Participatory Practice Guidelines, these resources include templates, checklists, and training tools, as well as a link to a four-month online training course about the guidelines.

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# Good Participatory Practice: Guidelines for Biomedical HIV Prevention Trials. Second edition.

This 88-page document outlines good participatory practice (GPP) guidelines and systematic guidance on how trial funders, sponsors, and implementers can effectively engage with all stakeholders in the design and conduct of biomedical HIV prevention trials. The GPP guidelines are divided into three main sections: the importance of and need for GPP in biomedical HIV prevention trials, guiding principles of GPP, and optimal GPP practices for biomedical HIV prevention trials.

- ## Community Partners Training Materials

Materials for educating community advisory board members about the clinical research process and their role in it include PowerPoint slides and instructor notes, a participant guide, workshop activities, handouts, and an instructor's guide.

## Country Experiences



Clinical research on microbicides has been conducted in

more than a dozen countries, and implementation research is beginning in a growing number of countries to prepare for microbicide introduction. This section provides resources that describe countries' experiences with microbicide development and implementation research. Case studies on microbicide introduction will be added as they become available.

Clinical Research

Implementation Research

# Clinical Research

Resources:

- **Gabi's Gift (CAPRISA 004 Video)**

This five-minute video follows one woman from the beginning of her participation in the CAPRISA 004 study of tenofovir gel to her joy when hearing the results.

# Implementation Research

Resources:

- **Rolling Out Tenofovir Gel in Family Planning Clinics: The CAPRISA 008 Implementation Trial (Abstract)**

CAPRISA 008 was a two-arm, open-label, randomized controlled, non-inferiority implementation trial that provided participants from CAPRISA 004 with post-trial access to tenofovir gel while generating evidence that could be used for future implementation of topical pre-exposure prophylaxis (PrEP) among women. Its findings on the delivery of a microbicide containing tenofovir gel in family planning clinics are reported in this chapter of a book about HIV prevention and treatment trials conducted by the Centre for the AIDS Programme of Research in South Africa.

- **Policy And Programme Considerations For ARV-Based Prevention For Women: Insights From Key Opinion Leaders In Zimbabwe About Tenofovir Gel**

This report describes the process and outcomes of a systematic inquiry among key opinion leaders in Zimbabwe about program and policy considerations to address in preparation for the potential introduction of tenofovir gel. Most respondents were supportive of introducing tenofovir gel should it prove effective, with several caveats, and safety and efficacy were the chief concerns of all respondents.

- **Communicating about Microbicides with Women in Mind: Communication Strategy and Adaptation Guide**

This final report for the Communicating about Microbicides with Women in Mind project was written to: 1) document the promise of vaginal microbicide gel as a new HIV prevention product for women, 2) describe the project's experience with materials development, 3) provide a sample microbicide communication strategy for Kenya, and 4) outline a process for updating and adapting the materials for use in other countries or with other new HIV prevention methods. Copies of the materials, including English- and Swahili-language materials and other project documents, are shown in an annex to the report.

- **A Pocket Guide to Thinking about Gender & Vaginal Microbicides in South Africa**

FHI 360 and Sonke Gender Justice conducted a gender analysis in South Africa to identify gender-related barriers and opportunities to women's microbicide access and use and to make recommendations for addressing those barriers. This pocket card, created with input from the South African National AIDS Council (SANAC) Men's and Women's sectors, is designed to build support for a gender-integrated microbicides rollout among community members and policy makers.

- **Program and Policy Considerations for Tenofovir Gel in India**

A program brief summarizes the findings of a landscape analysis conducted in India as part of a process developed by the Population Council to help policymakers and program managers identify the most strategic opportunities for introducing tenofovir gel. Based on a desk review and interviews with key decision makers, the brief reviews the epidemiologic context of the HIV epidemic, highlights policies and programs related to HIV, and provides other information relevant to potential introduction of tenofovir vaginal gel in India.

- **Setting the Stage for ARV-Based Prevention for Women: A Snapshot of the Zimbabwean Context**

A program brief summarizes the findings of a landscape analysis conducted in Zimbabwe as part of a process developed by the Population Council to help policymakers and program managers identify the most strategic opportunities for introducing tenofovir gel. Based on a desk review and interviews with key decision makers, the brief reviews the epidemiologic context of the HIV

epidemic, highlights policies and programs related to HIV, and provides other information relevant to potential introduction of tenofovir vaginal gel in Zimbabwe.

- **CAPRISA 008**

This webpage describes a follow-up study to the CAPRISA 004 tenofovir gel trial, CAPRISA 008, which assessed the feasibility and effectiveness of distributing tenofovir gel through family planning clinics in communities where the CAPRISA 004 trial took place.

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**Source URL:** <http://live-toolkits.pantheonsite.io/toolkits/microbicides>