Microbicides Toolkit

Microbicides are topical agents that are being tested to help prevent the sexual transmission of HIV. Vaginal microbicides are intended as an HIV prevention option for women, especially those who may have trouble negotiating condom use with their sexual partners. Rectal microbicides, which could be used by both men and women to reduce the risk of HIV infection during anal sex, are also being developed.

The most widely studied microbicides have been formulated as gels that are used either daily or before and after sex. However, other microbicide products, such as vaginal rings, can release an active drug over time. Most of the microbicides under study employ antiretroviral drugs that are commonly used in pill form to *treat* an HIV infection.

Antiretroviral pill formulations are also being studied for HIV prevention in an approach called pre-exposure prophylaxis (PrEP). On July 16, 2012, the U.S. Food and Drug Administration approved the use of a combination of the antiretroviral drugs tenofovir disoproxil fumarate and emtricitabine (TDF/FTC, or Truvada) for daily use as PrEP to reduce the risk of HIV infection in uninfected men and women who are at high risk of HIV infection and who may engage in sexual activity with HIV-infected partners.

This toolkit provides information about microbicides for health policymakers, program managers, community educators, trainers, advocates and communication specialists. Although microbicides are not yet available, this toolkit can help the reader develop implementation strategies once they come to the marketplace. This toolkit will be updated continually as the field progresses.

The introduction of microbicides will require a comprehensive approach, including:

- Knowledge of recent research results
- Up-to-date policies and guidelines

- Effective communication and marketing
- Quality training, supervision, and services
- Proper logistics

The thematic navigation tabs (listed above) provide the basic information, tools, and resources you will need to understand and introduce microbicides once they become available.

Are there new resources or topic areas that should be included in this toolkit? Share your suggestions, comments, and questions by emailing us at toolkits@k4health.org [1] or sending a message through the feedback form [2].

To find out whether a resource has already been included in this toolkit, visit the site map [3] or type the title in the search box. Visit the About page [4] for more detailed information about the selection of resources, a list of publishers, and other K4Health toolkits.

About:
What are K4Health Toolkits?

What is the purpose of this toolkit?

Who developed this toolkit?

Who are the publishers of the resources?

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Who are the intended audiences?

How do I get started using this toolkit?

What are K4Health Toolkits?

K4Health Toolkits are electronic collections of carefully selected information resources on a particular topic for health policy makers, program managers, and service providers. They are based on a continuous publishing principle that allows them to evolve after publication to capture additional resources and to identify and fill remaining information gaps.

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 mcirobicides.

- 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). If you do use these tools or adapt them, we would love to hear from you. Please e-mail us [1].

How can I suggest a resource to include in this toolkit?

We invite you to contribute to evolving and enhancing this toolkit. If you have developed or use quality resources that you think should be included in this toolkit, please share your suggestions through the feedback form [2]. The toolkit collaborators will review and consider your suggestions.

How can I make a comment or give feedback?

If you have comments about the toolkit, please use the feedback form [2]. Your feedback will help to ensure the toolkit remains up-to-date and is continually improved. For example, you can share ideas about how you have used the toolkit in your work so that others can learn from and adapt your experiences.

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 [5]

Alliance for Microbicide Development [6]

AmFAR [7]

AVAC [8]

Centers for Disease Control and Prevention (CDC) [9]

Centre for the AIDS Programme of Research in South Africa (CAPRISA) [10]

Coalition Advancing Multipurpose Innovations (CAMI) [11]

CONRAD [12]

EngenderHealth [13]

FHI 360 [14]

Gilead Sciences, Inc. [15]

Global Campaign for Microbicides (GCM) [16]

HIV/AIDS Network Coordination (HANC) [17]

HIV Prevention Trials Network (HPTN) [18]

HIV Vaccines and Microbicides Research Tracking Working Group [19]

International AIDS Vaccine Alliance [20]

International Partnership for Microbicides (IPM) [21]

International Rectal Microbicides Advocates (IRMA) [22]

Johns Hopkins Bloomberg School of Public Health [23]

Joint United Nations Programme on HIV/AIDS (UNAIDS) [24]

Kaiser Family Foundation [25]

London School of Hygiene and Tropical Medicine [26]

Microbicide Trials Network [27]

Microbicides Development Programme [28]

Microbicides Media and Communications Initiative

O'Neill Institute for National and Global Health Law, Georgetown University [29]

PATH [30]

The Population Council [31]

Rockefeller Foundation Microbicide Initiative [32]

The Wellcome Trust [33]

Setshaba Research Centre [34]

South African Medical Research Council [35]

Southern African HIV Clinicians Society Consensus Committee

Starpharma [36]

United Nations Development Programme [37]

University of Cape Town [38]

University of KwaZulu-Natal [39]

University of North Carolina at Chapel Hill [40]

U.S. Agency for International Development [41]

U.S. Food and Drug Administration [42]

U.S. National Institute of Allergy and Infectious Diseases [43]

Wits Reproductive Health and HIV Institute [44]

World Health Organization [45]

Essential Knowledge

In 2010, the Centre for the AIDS Programme of Research in South Africa (CAPRISA) showed that a vaginal gel containing tenofovir (a widely available antiretroviral drug) was safe and reduced a woman's risk of becoming infected with HIV by 39 percent. This was the first study to demonstrate the effectiveness of a topical microbicide, and it was an important milestone in the field of HIV prevention. Studies are under way to confirm the results of the tenofovir gel trial, and additional vaginal and rectal microbicide candidates are moving down 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 even 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.

Do you have a comment about this section or a resource you'd like to suggest? Please visit the feedback form [2].

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 has 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. Additional studies have shown that early treatment of HIV-infected individuals with oral ARV drugs can dramatically reduce the risk of transmission to an uninfected partner. This strategy is widely known as treatment as prevention. Information about ARV-based microbicides and the use of ARV drugs as PrEP can also be found in this section.

Research is also 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 or be delivered via diaphragms and vaginal rings to prevent both pregnancy and HIV. This section also includes the most up-to-date information on the development of these technologies.

Overview

Resources:

- ## Microbicides

  This fact sheet explains what microbicides are and provides a brief overview of microbicide research, including current and planned trials.

- ## Rectal Microbicides

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

- ## Microbicide Overview

  This document provides an overview of the worldwide AIDS epidemic and includes information on how microbicides are tested for safety and efficacy and how local communities can be involved in the research process. Recent advances in HIV prevention research, including the use of oral antiretroviral drugs to prevent new HIV infections, are also included.

- ## 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 70-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.

- ## Frequently Asked Questions about Microbicides

  Many common questions about microbicides are answered in this fact sheet, including what they are, when they might be available, and who is working on microbicide research and development.

- ## From Promise to Product: Advancing Rectal Microbicide Research and Advocacy

  From Promise to Product features recommendations on how to advance rectal microbicide research and advocacy. Global challenges to preventing HIV during sexual intercourse and the state of rectal microbicide research are also highlighted.

- ## Rectal Microbicides 101

  This comprehensive fact sheet contains information on what rectal microbicides are, why they are needed, who needs them, and challenges to their research and development.

- ## Prevention Research E-Learning Center: Microbicides Essentials

  Available online or via CD-ROM, this interactive multimedia course is intended to help a wide range of stakeholders answer questions about microbicides and the complexities of their development. It includes both basic and more nuanced information about microbicides. Users can receive continuing education credit for completing the course.

- ### Biomedical Interventions: Microbicides

  AIDSTAR-One's online HIV Prevention Knowledge Base includes a section that provides background information about microbicides and links to study summaries and tools.

Antiretroviral-Based Prevention

Resources:

- ### Update to Interim Guidance for Preexposure Prophylaxis (PrEP) for the Prevention of HIV Infection: PrEP for Injecting Drug Users

  After the release of the results [51] of a PrEP trial among injecting drug users in Thailand, the Centers for Disease Control and Prevention updated its interim guidance for health care providers in the United States, recommending that the preferred PrEP regimen for this population be a combination of tenofovir disoproxil fumarate and emtricitabine.

- ### 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.

- ### In Wake of Latest Trial Results, CDC Stresses that Consistent Use Is Imperative When Using Pre-exposure Prophylaxis to Prevent HIV Infection

  In a statement on the results of VOICE (Vaginal and Oral Interventions to Control the Epidemic), the director of the Division of HIV/AIDS Prevention at the U.S. Centers for Disease Control and Prevention (CDC) notes that both drug regimens evaluated in the trial have been

shown to be highly effective when taken consistently. He emphasizes that the VOICE results reinforce the need for physicians to closely follow the CDC's interim guidance on PrEP for heterosexually active adults and men who have sex with men and counsel patients about the need for high levels of adherence to daily PrEP regimens.

- ## FDA Approves First Drug for Reducing the Risk of Sexually Acquired HIV Infection

  This press release announces that the U.S. Food and Drug Administration has approved the use of Truvada (emtricitabine/tenofovir disoproxil fumarate) to reduce the risk of HIV infection in uninfected men and women who are at high risk of HIV infection and who may engage in sexual activity with HIV-infected partners. It also describes a risk evaluation and mitigation strategy (REMS) to minimize the risk that people using Truvada for pre-exposure prophylaxis will become infected with HIV and to reduce the development of drug resistance. Links to additional information are provided.

- ## Final Results of FEM-PrEP HIV-Prevention Study Indicate Great Attention to Adherence Will Be Required in PrEP Programs

  This press release announces the final results of the FEM-PrEP study, which was unable to determine whether daily use of the antiretroviral drug Truvada could reduce the risk of HIV infection because of low adherence to the drug regimen among study participants. The results of the study, published online July 11 in the New England Journal of Medicine, demonstrate that achieving high adherence will be a key factor in successful implementation of pre-exposure prophylaxis.

- ## Guidance on Oral Pre-exposure Prophylaxis (PrEP) for Serodiscordant Couples, Men and Transgender Women Who Have Sex with Men at High Risk of HIV: Recommendations for Use in the Context of Demonstration Projects

  Noting the need for experience with pre-exposure prophylaxis outside the controlled context of a clinical trial, the World Health Organization provides guidance on the daily use of antiretroviral drugs for HIV prevention by uninfected individuals participating in demonstration projects.

- ## Pre-Exposure Prophylaxis (PrEP)

  This fact sheet provides background information on why oral pre-exposure prophylaxis (PrEP) is important and discusses the results of recent PrEP trials. It also describes the antiretroviral drugs and regimens that are being tested as oral PrEP in a variety of populations, including heterosexual women and men, transgender women, men who have sex with men, and injection drug users.

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Southern African Guidelines for the Safe Use of Pre-Exposure Prophylaxis in Men Who Have Sex with Men Who Are at Risk for HIV Infection

These guidelines explain what pre-exposure prophylaxis (PrEP) is, provide current 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.

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Initiation of Antiretroviral Treatment Protects Uninfected Partners from HIV Infection (HPTN 052)

This press release describes the results of the HPTN 052 trial, which showed that early treatment with antiretroviral drugs could dramatically reduce the risk of transmission from an HIV-positive partner to an uninfected partner. HPTN 052 was the first study to prove that treatment of HIV-positive individuals (treatment as prevention) can be a form of pre-exposure prophylaxis.

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Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV Infection in Men Who Have Sex with Men

Interim guidance for health care providers in the United States is provided based on the results of iPrex, a large clinical trial testing the efficacy and safety of pre-exposure prophylaxis for reducing HIV acquisition by men who have sex with men. The document is intended to guide clinical practice until comprehensive U.S. Public Health Service guidelines are available.

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Interim Guidance for Clinicians Considering the Use of Preexposure Prophylaxis for the Prevention of HIV Infection in Heterosexually Active Adults

This interim guidance for health care providers in the United States includes consideration of the results of trials of pre-exposure prophylaxis (PrEP) among heterosexual women and men, as well as the U.S. Food and Drug Administration’s approval of the use of Truvada as PrEP by men and women at high risk of HIV infection. The guidance also addresses pregnancy and safety issues that were not discussed in the previous interim guidance for the use of PrEP in men who have sex with men (see below).

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PrEP Watch

PrEP Watch provides updates, background information on pre-exposure prophylaxis and the U.S. Food and Drug Administration’s review process, and commentary from a broad coalition of AIDS organizations.

- ### Treatment as Prevention

  This web page provides background information on HIV treatment as prevention for uninfected partners, as well as links to answers to frequently asked questions, trial updates, and slide presentations.

Multipurpose Prevention Technologies

Resources:

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

  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.

- ### Global Forum on Multipurpose Prevention Technologies for Reproductive Health: Advancing the MPT Agenda. Meeting Report

  The final report of a two-day global forum with more than 60 diverse experts describes how they reviewed and debated existing evidence and new ideas for developing and delivering multipurpose prevention technologies. Participants proposed and committed to taking a number of concrete next steps to advance the field, underscoring the potential of multipurpose technologies that meet multiple sexual and reproductive health needs to improve women’s health.

- ### MPT Microbicides and Devices Database

  This web page highlights the Multipurpose Prevention Technologies (MPT) Microbicides and Devices Database, which contains both available and emerging multipurpose prevention technologies for sexual and reproductive health. The database outlines indications and other product information and provides links for further information on each multipurpose prevention technology.

- ### Multipurpose Prevention Technologies

  CONRAD's work in developing multipurpose prevention technologies to prevent pregnancy, HIV infection, and other sexually transmitted infections is described on this web page. A bibliography on multipurpose prevention technologies is included.

- ### Multipurpose Prevention Technologies: Biomedical Tools to Prevent HIV-1, HSV-2, and Unintended Pregnancies

  A link to a 10-page review article on existing and novel approaches to multipurpose prevention strategies, published in the journal Infectious Diseases in Obstetrics and Gynecology, is provided. The authors conclude that the challenge is to refine these products to make them more potent, convenient, accessible, and acceptable.

- ### USAID Support for Multipurpose Prevention Technologies: Past, Present, Future

  This presentation provides an overview of the Multipurpose Prevention Technologies Initiative of the U.S. Agency for International Development (USAID) and highlights the initiative's current and planned activities. USAID supports a range of partners working on multipurpose prevention technologies, including CONRAD, the Population Council, PATH, the International Partnership for Microbicides, and FHI 360 (formerly Family Health International).

- ### Saving Lives with Multipurpose Prevention Technologies

  This 24-page brief draws from an international symposium on multipurpose prevention technologies held in Berkeley, California, in March 2009. "Advancing Prevention Technologies for Sexual and Reproductive Health" brought together more than 150 reproductive health researchers and advocates to discuss and debate opportunities and challenges for advancing technologies that address multiple reproductive health indications. The brief concludes with specific recommendations to help the global health community accelerate access to these technologies.

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:

The Rectal Revolution is Here

"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.

Giving Women Power Over AIDS

The International Partnership for Microbicides provides a brief introduction to the unequal impact of the HIV/AIDS epidemic on women, the promise of microbicides as a woman-controlled method, and the essential role microbicides could play in achieving the United Nation's Millennium Development Goals.

Microbicides for Pregnant and Breastfeeding Women

The Microbicide Trials Network research program to determine whether tenofovir gel can safely and effectively protect women against HIV when they are pregnant or breastfeeding is summarized in this fact sheet. The current knowledge on this topic is also summarized, and four clinical trials of microbicides in this population of women are briefly described.

Women and the Need for Microbicides

The urgent need for woman-initiated HIV prevention options and how such options could complement other prevention approaches are discussed in this fact sheet.

HIV/AIDS and the Millennium Development Goals: Microbicides and the Need for Long-Term Prevention

Despite the availability of multiple HIV prevention options, women continue to be disproportionally affected by HIV throughout the world. This short document emphasizes the urgent need for HIV prevention options that women can control. It also discusses how microbicides could help meet the United Nation's Millennium Development Goals by 2015.

Microbicides: What Do They Mean for Women?

General information about microbicides, as well as more specific information about the advantages of microbicides for women, is provided in this fact sheet. Questions and concerns women have raised about the products are also addressed.

Rectal Microbicides 101

This comprehensive fact sheet contains information on what rectal microbicides are, why they are needed, who needs them, and challenges to their research and development.

Status of Microbicide Research

AVAC regularly updates the following resources, which summarize the status of current trials of microbicides and other HIV prevention technologies. See the Clinical Research section [52] of this toolkit for additional information on the clinical research process.

Resources:

- ### Ongoing Clinical Trials of Topical Microbicide Candidates

  The microbicide clinical trials that are under way are presented in a table that includes the name of each study, sponsorship information, start and expected end dates, study locations, and additional details.

- ### HIV Prevention Around the Globe

  An interactive world map displays the location of all current HIV prevention trials, including those for microbicides. Click on the name of a country to read a summary of trials and the HIV/AIDS statistics for that country.

- ### 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.

- ### HIV Prevention Research: Timeline of Expected Efficacy Trial Results

  Summaries and results of past HIV prevention trials are listed in chronological order along this interactive timeline. Ongoing trials and their expected dates of completion are also

included.

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:

- ## ARV-Based HIV Prevention: State of the Science and Considerations for Implementation

  This brief summarizes the discussions and take-home messages from a consultation convened by the Kenya National AIDS/STI Control Programme (NASCOP) and the Kenya Medical Research Institute (KEMRI), in conjunction with FHI 360, to consider the potential introduction of microbicides and pre-exposure prophylaxis (PrEP) for HIV prevention in Kenya. Stakeholders who met in Naivasha, Kenya, in November 2012 agreed that it is time to begin laying a foundation for the introduction of new and potential antiretroviral-based prevention methods in Kenya.

- ## Preparing for Access to Microbicides and the Dapivirine Ring for HIV Prevention: Preliminary Strategy

  This 37-page report describes a strategy designed to ensure rapid access by women in developing countries to any product that might prove successful in the Phase III trials of the International Partnership for Microbicides (IPM). Building on IPM's Strategic Plan 2011-2015, IPM used the dapivirine ring as a case study to develop an access strategy that will serve as a guide for IPM through product development and launch (2011-2018).

- ## USAID Proposal for a Shared Vision and Strategic Plan for Microbicide Introduction: Draft for Discussion

  The administrator of the U.S. Agency for International Development (USAID) identified the need for this strategy document after convening a high-level stakeholders' meeting in November 2010 to discuss how to expedite licensure and introduction of tenofovir gel should confirmatory studies yield positive results. USAID will actively seek additional feedback from a broad range of other stakeholders and incorporate it in future versions of the strategy. This process is intended to yield a shared vision for microbicide introduction in the broader context of HIV prevention and global health. The document describes seven high-priority strategy elements to be implemented in partnership with governments and stakeholders at the country level. A fact sheet provides additional information about the 2010 meeting and USAID support for microbicide development.

Microbicides: The Way Forward

A comprehensive overview of what had been learned about microbicides over the past several decades and the gaps in research that remained is provided in this 2010 strategy document. The document also recommends nine future priorities, including building on behavioral and social science research, revising cost profiles for microbicides, and evaluating all nine of the priorities on a regular basis.

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Bringing Microbicides to Market

This short fact sheet summarizes the steps needed to bring a microbicide to market. The entire process can take decades, as a product moves from laboratory research and clinical trials to manufacturing, marketing, financing, and distribution.

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Microbicide Planned Trials

Links to an up-to-date list of ongoing microbicide trials, along with instructions on how to use AVAC's HIV Prevention Research and Development Database to search for planned trials, are provided on this page.

Useful Links

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

AIDSTAR-One [5]

Alliance for Microbicide Development [6]

AmFAR [7]

AVAC [8]

Centers for Disease Control and Prevention (CDC) [9]

Centre for the AIDS Programme of Research in South Africa (CAPRISA) [10]

Coalition Advancing Multipurpose Innovations (CAMI) [11]

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University of North Carolina at Chapel Hill [40]

U.S. Agency for International Development [41]

U.S. Food and Drug Administration [42]

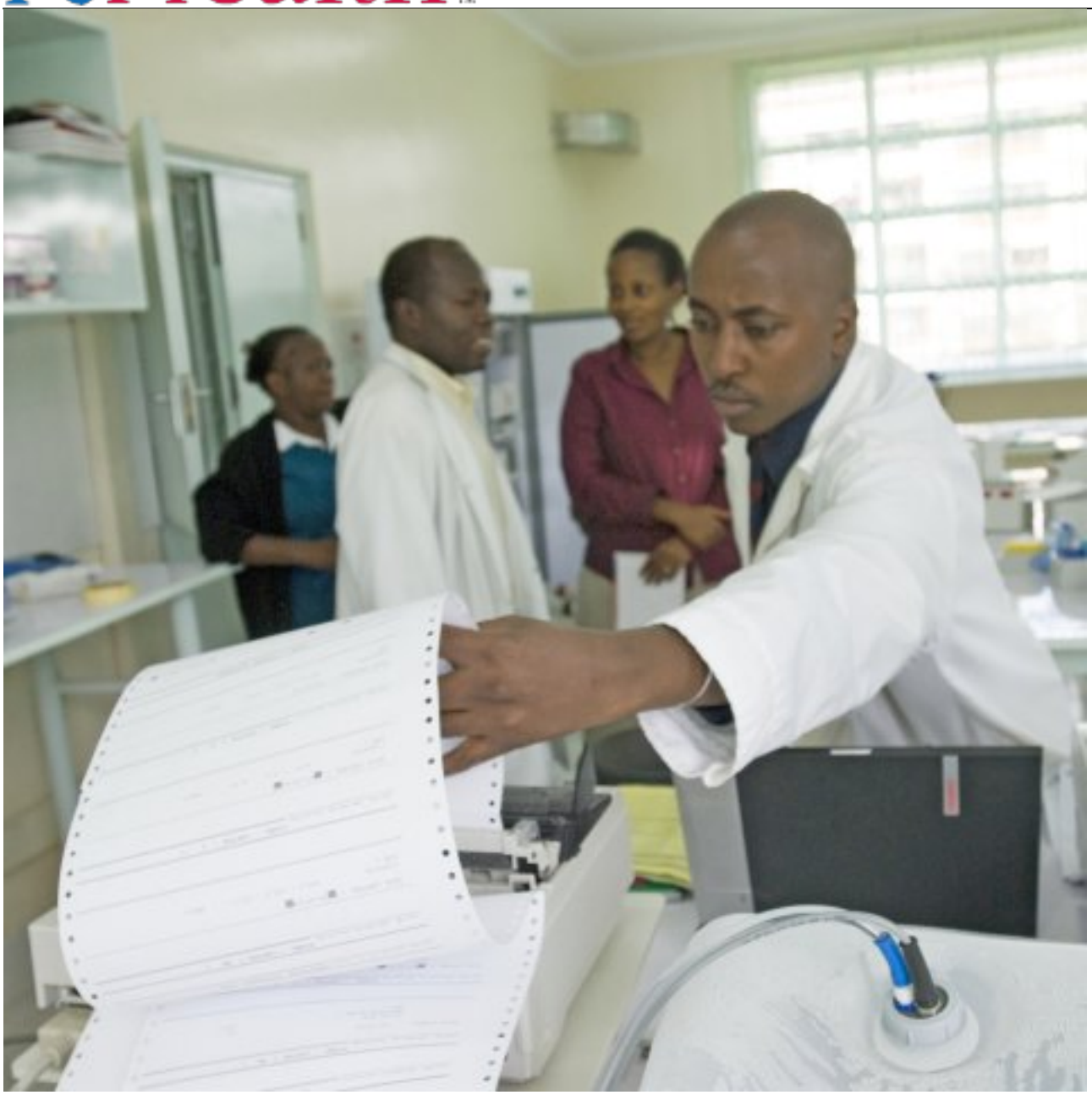
U.S. National Institute of Allergy and Infectious Diseases [43]

Wits Reproductive Health and HIV Institute [44]

World Health Organization [45]

Clinical Research

In the past 20 years, more than 30 candidate microbicides have been tested in clinical trials. Many have subsequently been ruled out as viable for further clinical study. The results of a trial that for the first time demonstrated the effectiveness of a microbicide were reported by the Centre for the AIDS Programme of Research in South Africa (CAPRISA) in July 2010 at the XVIIIth International AIDS Conference (AIDS 2010).



The CAPRISA study — showing that tenofovir gel used before and after sex reduced a woman's risk of becoming infected with HIV by 39 percent — was an important milestone in the field of HIV prevention. It was the first time that a drug used to treat HIV was shown to reduce the sexual transmission of HIV, with the potential to save millions of lives should the results be confirmed in other trials and the product then be made widely available.

The VOICE (Vaginal and Oral Interventions to Control the Epidemic) trial, which tested daily use of tenofovir gel, found that it was safe but not effective in preventing HIV. Other clinical trials continue to explore the safety and effectiveness of tenofovir gel and other candidate microbicides. This section contains resource materials that highlight the recent history of clinical research on these microbicides, including studies of candidates that are no longer being assessed (for various reasons) and active candidate 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 articles 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 the 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. In 2010, clinical research identified a vaginal gel containing tenofovir as the first effective microbicide for preventing HIV in women. Confirmatory research is under way. In 2011, a trial stopped testing a different regimen of tenofovir gel (daily use rather than before and after sex, as studied in the first trial) when an interim review of the data showed that this regimen was safe but not effective in preventing HIV among the women enrolled in the trial.

The results of all completed effectiveness (Phase IIb and Phase III) microbicide trials are listed below by study product. Additional products that are being evaluated are described on the Current and Planned Trials [54] page of the toolkit. For another up-to-date summary of microbicide effectiveness trials and their results, see AVAC's Microbicide Trials Results. [56]

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 gel

Resources:

- ## 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 [57], 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.

- ## A Cascade of Hope and Questions Volume 2: Understanding the Results of CAPRISA 004

  Understanding the Results of CAPRISA 004 is the second in AVAC's four-part series on antiretroviral-based HIV prevention. This comprehensive 10-page document discusses the results of the CAPRISA 004 trial both for HIV prevention and for the prevention of herpes simplex virus type 2. Follow-up research, regulatory preparation for 1% tenofovir gel, and the need for continued advocacy are also covered.

- ## 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 backgrounder, 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 gives a human face to the CAPRISA 004 trial by interviewing and following one woman from the beginning of her participation in the study to her joy when hearing the results.

PRO 2000

Resources:

- ## MDP 301 Quick Facts

  The MDP 301 Phase III trial evaluated the safety and effectiveness of the vaginal microbicide PRO 2000 for reducing the risk of HIV infection in women. From September 2005 to September 2009, 9,385 women enrolled in the study at six research centers in South Africa, Tanzania, Uganda, and Zambia. This two-page fact sheet provides an overview of the trial.

- ## MDP 301 Trial Results – Q&A

  Answers are provided to seven questions about the results of the MDP 301 trial, which evaluated the safety and effectiveness of the vaginal microbicide PRO 2000. Topics included in this three-page document are why testing of the 2% concentration was stopped in February 2008 and what the research achieved in determining that PRO 2000 was not effective in preventing HIV infection.

- ## Questions and Answers: HPTN 035

  Through a question-and-answer format, this four-page fact sheet explains HPTN 035, a multicenter clinical trial to evaluate the candidate microbicides BufferGel and PRO 2000 for prevention of HIV in women. Study results, namely that there were no statistically significant effects of the products, are included.

- ## Understanding the Intriguing Results from the HPTN 035 Trial

  Answers to important questions about the results of the HPTN 035 trial of the use Buffergel and PRO 2000 for prevention of HIV in women are provided in this document.

BufferGel

Resources:

- ## Questions and Answers: HPTN 035

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- ## Understanding the Intriguing Results from the HPTN 035 Trial

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Carraguard

Resources:

- ## Trial Shows Anti-HIV Microbicide Is Safe, but Does Not Prove It Effective

  This is a press release announcing that the Population Council's Phase III clinical trial of Carraguard found the product to be safe for vaginal use, but not effective in preventing male-to-female HIV transmission during vaginal intercourse.

- ## Clinical Studies: Carraguard Phase III Clinical Trial

  The results of the Phase III clinical trial of the Population Council's candidate microbicide, Carraguard, are presented. The trial, which began in March 2004 and was completed in March 2007 at three sites in South Africa, did not show that Carraguard is effective in preventing HIV transmission during vaginal sex.

Cellulose sulfate

Resources:

- ## Cellulose Sulfate Ruled Out as a Microbicide

  This research brief presents results of a randomized controlled trial testing the effectiveness of cellulose sulfate as a vaginal microbicide. The study, published in The New England Journal of Medicine, concluded that cellulose sulfate is unlikely to prevent the transmission of HIV and might even increase a woman's risk of HIV infection.

SAVVY

Resources:

- ## HIV-Prevention Studies of SAVVY Vaginal Gel Stopped Because of Futility

  This document announces the final results for two clinical trials — one in Nigeria and one in Ghana — that were closed early because a low incidence of HIV among the participants prevented scientists from detecting an effect of the candidate microbicide SAVVY. For statistical reasons, a continuation of either study could not have established SAVVY's ability to prevent HIV infection.

- ## Answering Hard Questions on the Savvy Trial Results

  Answers to difficult questions people may have had after the SAVVY trials were stopped early in Ghana and Nigeria are provided in this four-page fact sheet.

Current and Planned Trials

The research pipeline contains microbicide products at all stages of the research process. Tenofovir

gel continues to be tested in different study populations and in different contexts, including its use as a rectal microbicide. Newer products, such as dapivirine and VivaGel, and new delivery methods such as vaginal rings are also being evaluated for their safety and effectiveness.

The links below include information on specific ongoing or planned microbicide trials. For the most up-to-date summaries of all current trials, see AVAC's Ongoing Clinical Trials of Topical Microbicide Candidates [58], HIV Prevention Research and Development Database [59], and Px Wire: A Quarterly Update on HIV Prevention Research [60]. For more information on planned trials, including some that are not listed below, see AVAC's Microbicide Planned Trials [61]. Additional information about trials by research organization is provided in International Partnership for Microbicides (IPM) Clinical Trials [62] and Ongoing and Planned Trials of the Microbicide Trials Network (MTN [63]).

Tenofovir gel (vaginal use)

Resources:

- ## Development of Microbicide Gel to Prevent HIV Transmission in Women: Announcement of Follow-on Trial

  This press release announces the development of the Follow-on African Consortium for Tenofovir Studies FACTS) partnership, which will conduct another multicenter Phase III trial to test the safety and effectiveness of 1% tenofovir gel (used before and after sex) for preventing HIV in women. Led by Dr. Helen Rees, the director of the Wits Reproductive Health and HIV Institute, the trial will be known as FACTS 001. Additional evidence from this study is needed before tenofovir gel can be licensed for HIV prevention.

- ## Researchers Take Another Step Closer to HIV Prevention Product for Use During Pregnancy

  In a press release, the Microbicide Trials Network announces a Phase I clinical trial, under way at two U.S. sites — Magee-Women's Hospital of the University of Pittsburgh Medical Center and the University of Alabama, Birmingham. The trial aims to determine if the vaginal microbicide tenofovir gel is safe for women to use while pregnant or breastfeeding.

- ## Tenofovir Gel: Preparing for Implementation in the Health Service: The CAPRISA 008 & 009 Trials

  A PowerPoint presentation by Dr. Salim Abdool Karim, Director of the Centre for the AIDS Programme of Research in South Africa (CAPRISA), describes two follow-on trials to CAPRISA 004. CAPRISA 008 is providing CAPRISA 004 participants with post-trial access to tenofovir, collecting additional safety data, and evaluating a model for providing tenofovir through family planning services. CAPRISA 009 is determining whether exposure to tenofovir gel will change a woman's therapeutic response to antiretroviral treatment that contains tenofovir. Both studies will facilitate the eventual introduction of tenofovir gel into health facilities in South Africa.

Other tenofovir gel formulations (rectal use)

Resources:

- ## Backgrounder: MTN: Phase II Safety and Acceptability Study of Tenofovir Gel Reformulated for Rectal Use

  MTN-017 is a Phase II trial evaluating the rectal safety and acceptability of a tenofovir gel reformulated with reduced glycerin. This short document provides an overview of the study and also describes its importance, how it is being conducted, and how the safety of participants is being monitored. The trial will enroll about 186 men who have sex with men and transgendered women at sites in the United States, Peru, South Africa, and Thailand.

- ## Tenofovir Gel Provides High Level of Protection against HIV in Rectal Tissue

  This press release reports on an early-phase study, presented at the 18th Conference on Retroviruses and Opportunistic Infections, which found that a gel developed to protect against HIV during vaginal sex produced a strong antiviral effect when used in the rectum. The study, conducted at the University of California, Los Angeles (UCLA) and the University of Pittsburgh and known as RMP-02/MTN-006, is the first clinical trial of tenofovir gel for rectal use.

Dapivirine

Resources:

- ## 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. The trial will enroll about 3,476 women at several sites in Africa. The dapivirine vaginal ring was developed by the International Partnership for Microbicides.

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Phase III Sister Studies of a Microbicide Ring to Prevent HIV: ASPIRE and The Ring Study

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 are designed to determine whether monthly use of a vaginal ring that delivers the antiretroviral drug dapivirine helps prevent HIV infection in women and is safe for long-term use.

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The Ring Study

This page on the website of the International Partnership for Microbicides provides information and links to other 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 is expected to enroll 1,650 women ages 18 to 45 across six sites in South Africa, Rwanda, and Malawi.

-

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 gel, a ring, and a ring combining dapivirine with another potential microbicide.

VivaGel (SPL7013 gel)

Resources:

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VivaGel

VivaGel (SPL7013 gel) is a candidate vaginal microbicide gel being developed and tested for the prevention of HIV, herpes simplex virus type 2, and other sexually transmitted infections. It is also being tested for its ability to prevent and treat bacterial vaginosis. This short introduction to the product contains links to more information about VivaGel, including some ongoing clinical trials.

-

MTN 004

MTN-004, a Phase I, two-arm, two-site, randomized, double-blind, placebo-controlled trial evaluating the safety, acceptability, and ease of use of the microbicide candidate VivaGel (SPL7013 Gel) in sexually active, HIV-negative women ages 18 to 24, is described in this document. MTN-004 found that VivaGel was generally well tolerated, but participants said it was less acceptable for use than the two placebo gels. The placebo gels were a VivaGel placebo, formulated in the same way but without the active ingredient, and a placebo known as hydroxyethylcellulose, which also contains no active microbicide. The findings suggest that it may be necessary to consider reformulating VivaGel before moving to further studies.

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 to evaluate its effectiveness in preventing HIV and, sometimes, other sexually transmitted infections. 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, community engagement, 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.

Because many of these issues are also relevant to implementation research, you can find related and additional information in the Implementation Research [64] section of the toolkit.

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:

- ## HIV Prevention Trials Network Ethics Guidance for Research

  This 50-page document, written primarily for use within the HIV Prevention Trials Network (HPTN), aims to facilitate HPTN's mission of conducting HIV prevention research at the highest scientific and ethical standards by raising awareness of the associated ethical considerations, engaging network members at all levels in discussion about those considerations, and facilitating the integration of ethical considerations into the design and implementation of HPTN research. It is organized sequentially according to the different stages of HIV prevention research, from pre-research preparations, to implementation of research protocols, to activities after data are collected.

- ## 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.

- ## Research Ethics Training Curriculum

  The Research Ethics Training Curriculum, available in a Flash version or as a downloadable 444-page PDF, has been developed for an international audience of researchers and research ethics committee members who design or implement research that includes human participants or who conduct reviews of the ethical aspects of research. The training curriculum includes an overview of the main ethical principles to be considered in the development and conduct of research involving human participants; guidance to assist researchers in designing studies that are respectful of local cultures, regulations, and expectations; case studies for considering

  real-world examples of ethical issues; and ancillary reference documents on modern perspectives that shape the research ethics field. French, Portuguese, and Spanish versions of the first edition are available.

- ## Informed Consent in HIV Prevention Trials: Report of an International Workshop

  The presentations and discussions from an international workshop that drew together more than 70 participants from 11 countries and varied backgrounds are summarized in this 65-page report. The workshop underscored the dynamic and creative way that clinical trial sponsors and investigators, clinic staff, social science researchers, donors, and communities are approaching the challenge of informed consent in these complex and critical HIV prevention trials.

- ## Research Ethics Training Curriculum for Community Representatives

  Developed and field-tested in eight countries, the Research Ethics Training Curriculum for Community Representatives helps community representatives understand the research process and their roles and responsibilities as partners of the research team. The curriculum also explains the corresponding roles and responsibilities of researchers and of ethics committees and institutional review boards.

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.

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.

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.

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 will affect other trials.

Community Partners Training Materials

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

Recommendations for Community Involvement in National

Institute of Allergy and Infectious Diseases HIV/AIDS Clinical Trials Research

This announcement introduces a 60-page document that 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 full document, an executive summary, and an executive summary in Spanish are included.

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 groups known as data 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 recent situations in which a data safety monitoring board has made a recommendation that affected the conduct of a trial are reviewed.

- ### Evaluating the Safety of Vaginal Microbicides: The Fundamentals

  Part of a series intended to serve as a resource for non-scientists, this brief addresses how the safety of vaginal microbicides is evaluated and the strengths and limitations of various evaluation methods.

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:

- ## 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.

- ## 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.

- ### Adherence and its Measurement in Microbicide Trials

  This eight-page executive summary provides an overview of themes, pertinent conclusions, and key actions presented and discussed at a meeting held in December 2007 in Washington, DC. The document provides the main points of each presentation and closes with key findings emerging from those presentations and associated discussions.

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.

- ### Questions and Answers: MTN-009: The HIV Drug Resistance Study

  The MTN-009 study is determining the prevalence of HIV drug resistance among women in South Africa, where the risk of HIV is very high. This document from the Microbicide Trials Network not only explains the study in more detail but also answers a variety of questions about how drug resistance develops, how common it is, and how it can be measured.

- ### 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.

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HIV Drug Resistance and ARV-Based Prevention (Video)

A presentation given by Dr. John Mellors at a meeting of the Microbicide Trials Network Community Working Group in Cape Town, South Africa, in June 2008 is excerpted in this video. It covers understanding HIV drug resistance, how resistance occurs, whether resistance can occur when antiretroviral drugs are used for prevention, and the precautions taken to avoid HIV resistance in the VOICE (Vaginal and Oral Interventions to Control the Epidemic) trial. It also includes a workshop exercise in which participants dramatize the development of resistance.

-

Understanding Resistance

This web page provides links to fact sheets and other resources about drug resistance and antiretroviral-based prevention, including diagrams that use graphics and simple language to explain HIV resistance to antiretroviral drugs. The diagrams address what resistance is, drug resistance and antiretroviral therapy, and the precautions taken to avoid resistance in the VOICE (Vaginal and Oral Interventions to Control the Epidemic) trial.

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 Counseling and Testing Training

This document describes a web-based training program for clinicians and counselors who work with study participants at global clinical research sites supported by the Division of AIDS within the National Institute of Allergy and Infectious Diseases. Learners can access a training resource manual, a study guide, and 10 interactive e-learning modules. They can also track their completion of the training and their performance on knowledge self-assessments.

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Microbicides Development Programme: Engaging the Community in the Standard of Care Debate in a Vaginal Microbicide Trial in Mwanza, Tanzania

This 12-page article, published online in BMC Medical Ethics, describes a community-focused approach to develop a locally appropriate standard of health care in the context of a Phase III vaginal microbicide trial in northwest Tanzania. Participatory methodologies enabled the development of effective partnerships between researchers, participant representatives, and community stakeholders and facilitated local dialogue and consensus on what constitutes a locally appropriate standard of health care.

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Standards of Prevention in HIV Prevention Trials: Consultation Report and Recommendations

Summarized in this 40-page report are the key background presentations, discussions, exercises, and main issues that emerged during a consultation that brought together nearly 60 researchers, advocates, ethicists, donors, policymakers, and regulators working in HIV prevention. The consultation was designed to build on the existing guidelines from the Joint United Nations Programme on HIV/AIDS and the World Health Organization, to explore challenges in operationalizing the guidance, and to derive a set of criteria to help apply the guidance in practice.

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Consultation on Operationalizing Access to HIV Treatment and Care

Thirty stakeholders gathered for a two-day brainstorming session in Washington, DC, to explore ways to provide a uniform HIV-specific care and treatment package for individuals who seroconvert while participating in an HIV prevention trial. The 24-page report of the meeting says that participants endorsed the idea of empowering a small working group to develop a draft proposal for operationalizing access to treatment and care.

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Ensuring Care Through Adequate Referrals and Community Partnerships for Women Participating in HIV Prevention Trials: Experience from the Phase III Carraguard™ Trial in Isipingo, Kwazulu Natal, Durban, South Africa

The South African Medical Research Council describes the strategies used to make enhanced standard of care options available to women screened out due to HIV and seroconversion or pregnancy post-enrollment in the Phase III Carraguard trial conducted in Isipingo, KwaZulu Natal, South Africa. Methodology, results, and conclusions are presented.

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Establishing the Standard of Care in HIV Prevention Trials: Experience of Setshaba Research Centre

The experience of the Setshaba Research Centre with a Phase III Carraguard trial completed in 2007 is presented. This slide presentation outlines the standard of care for all participants, those who were HIV-positive, and those who seroconverted. It also identifies lessons learned along the way.

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 the new microbicide be integrated into local health services? Will the microbicide be accepted by the general public? What is the most cost-effective way to distribute the microbicide? Will drug resistance become an issue after long-term use of the microbicide?

Such questions are currently being addressed in several investigations. The CAPRISA 008 study, for example, is exploring a model of distributing tenofovir gel through family planning clinics and is developing a toolkit to help clinics implement the delivery of tenofovir gel. CAPRISA 009 is studying whether exposure to tenofovir gel might cause resistance to antiretroviral treatments that contain tenofovir. Many unanswered questions remain, and additional studies are planned.

Preparing for Introduction **[65]**

Acceptability and Affordability **[66]**

Impact and Cost-effectiveness **[67]**

Access and Delivery [68]

Preparing for Introduction

The acquisition of information is the key to preparing to introduce and expedite access to microbicides should they prove effective in trials. 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:

- ## AVAC Report 2011: The End?

  This web page provides links to a 48-page report (and individual sections of the report) from AVAC outlining a three-part, science-based agenda to end the AIDS epidemic. The agenda consists of these priorities: deliver today's proven strategies at scale for immediate impact; demonstrate and roll out newly available HIV prevention tools, including pre-exposure prophylaxis and microbicides, for even greater impact in five to ten years; and develop long-term solutions — including an effective vaccine and a cure — that will make it possible to "close the door on AIDS."

- ## CAPRISA 004 after Vienna: Advancing the Tenofovir Gel Development Agenda

  Quarraisha Abdool Karim, PhD, one of the two principal investigators of the CAPRISA 004 trial, outlines next steps for reducing HIV in women with tenofovir gel in this PowerPoint presentation. The presentation addresses regulation, access, implementation, and enhancing effectiveness.

- ## Next Steps for 1% Tenofovir Gel: Meeting Report

  This is a four-page executive summary of a meeting that the World Health Organization and the Joint United Nations Programme on HIV/AIDS convened in August 2010, which drew together more than 80 diverse stakeholders from a range of countries to identify gaps and develop consensus on priority research to confirm the safety, effectiveness, and acceptability of 1% tenofovir gel; develop the most efficient pathways for licensure and development of guidelines; delineate priorities, next steps, and primary responsibilities in clinical research, programmatic research, and regulatory submission; agree on mechanisms for coordination and execution; and identify funding sources and gaps.

- ## USAID Proposal for a Shared Vision and Strategic Plan for Microbicide Introduction: Draft for Discussion

The administrator of the U.S. Agency for International Development (USAID) identified the need for this strategy document after convening a high-level stakeholders' meeting in November 2010 to discuss how to expedite licensure and introduction of tenofovir gel should confirmatory studies yield positive results. USAID will actively seek additional feedback from a broad range of other stakeholders and incorporate it in future versions of the strategy. This process is intended to yield a shared vision for microbicide introduction in the broader context of HIV prevention and global health. The document describes seven high-priority strategy elements to be implemented in partnership with governments and stakeholders at the country level. A fact sheet provides additional information about the 2010 meeting and USAID support for microbicide development.

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Microbicides: The Way Forward

A comprehensive overview of what had been learned about microbicides over the past several decades and the gaps in research that remained is provided in this 2010 strategy document. The document also recommends nine future priorities, including building on behavioral and social science research, revising cost profiles for microbicides, and evaluating all nine of the priorities on a regular basis.

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Towards Microbicide Rollout in sub-Saharan Africa: Ensuring Microbicides are an Effective Tool for HIV Prevention and Women's Empowerment

This brief discusses four central issues in ensuring that microbicides become a tool for HIV prevention and women's rights: 1) What level of efficacy should be attained before a microbicide is introduced as a viable prevention option? 2) Should microbicides, once available, be free at the point of access for women? 3) How do we bring men into the conversation about microbicide use, while still empowering women? 4) How can microbicides be marketed in ways that do not stigmatize them or the women who use them?

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Paving the Path: Preparing for Microbicide Introduction

In this 75-page report, results are presented from a qualitative study that explored a range of issues likely to influence microbicide introduction — positively or negatively — at three levels: community, health service, and policy. The study identified critical issues to be addressed in building support for microbicides and facilitating smooth introduction.

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:

- ## 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.

- ## 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.

- ## 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.

- ## The Role of Partnership Dynamics in Determining the Acceptability of Condoms and Microbicides (abstract)

  During the pilot study for the MDP 301 Phase III trial, in-depth interviews were conducted and data from 45 couples at five sites in South Africa were analyzed using a grounded theory approach. Findings revealed that, although gel was designed to be "woman-controlled," men exercised considerable influence in determining whether and how gel was used. Negotiations about gel use were largely successful. These results are summarized in this abstract for an eight-page paper published in AIDS Care.

- ## Financing Mechanisms for Microbicide R&D and Future Introduction

  This 49-page report uses a scenario-planning approach to explore the potential costs of introducing future microbicides. The approach is based on assumptions about countries that are likely to be among the first to adopt a future product and on the actual introduction of other relevant health commodities aimed at a similar target population (sexually active women).

Impact and Cost-effectiveness

Different economic and cultural contexts will undoubtedly affect the impact and cost-effectiveness of

a microbicide. Researchers are considering a variety of situations in light of such factors. Models encompassing various scenarios have produced encouraging results: millions of HIV infections could be averted, and incidence of HIV significantly decreased by 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:

- ### Identifying Optimal Strategies for Microbicide Distribution in India and South Africa: Modelling and Cost-effectiveness Analyses

  This 60-page report presents the findings from a study that uses epidemiological modeling and economic analyses to explore the potential impact and cost-effectiveness of different microbicide introduction strategies in Southern India and South Africa.

- ### The Economics of Microbicides Development: A Case for Investment

  This 27-page report from the Pharmaco-Economics Working Group summarizes an analysis that was conducted to reduce some of the uncertainty about microbicide economics, thus helping to attract additional private investors and provide the donor community with valuable insight into the true financial cost of developing the current microbicide pipeline. Five appendices present additional data and discussion related to sizing the market, product pricing, market penetration, product development costs and timing, and return on investment.

- ### The Public Health Benefits of Microbicides in Lower-Income Countries: Model Projections

  A study that used epidemiological modeling and economic analysis to estimate the potential public health impact of the introduction of an effective microbicide in lower-income countries is described in this 58-page report. The findings suggest that even using relatively conservative assumptions about microbicide efficacy and coverage, the three-year cumulative impact of microbicide use could result in 2.5 million HIV infections averted among women, men, and children in lower-income countries. This could lead to a US$2.7 billion savings (in present-value terms) for health-system costs averted and an additional US$1 billion in productivity savings gained from preventing absenteeism and retraining and replacing workers.

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:

- ### Preparing for Access to Microbicides and the Dapivirine Ring for HIV Prevention: Preliminary Strategy

This 37-page report describes a strategy designed to ensure rapid access by women in developing countries to any product that might prove successful in the Phase III trials of the International Partnership for Microbicides (IPM). Building on IPM's Strategic Plan 2011-2015, IPM used the dapivirine ring as a case study to develop an access strategy that will serve as a guide for IPM through product development and launch (2011-2018).

- ## Planning for Microbicide Access in Developing Countries: Lessons from the Introduction of Contraceptive Technologies

  The introduction histories of three novel contraceptives — intrauterine devices, implants, and female condoms — are reviewed in this 34-page paper to glean valuable lessons for the introduction of microbicides.

- ## Microbicide Planned Trials: CAPRISA 008 and 009

  This document announces plans for two CAPRISA 004 tenofovir gel follow-up studies. One (CAPRISA 008) is assessing the feasibility and effectiveness of distributing tenofovir gel through family planning clinics in communities where the CAPRISA 004 trial took place. The other (CAPRISA 009) will compare treatment outcomes for those who are on combined antiretroviral treatment that includes tenofovir with those who are on combined antiretroviral treatment that does not include tenofovir.

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 **[69]**

National Policies **[70]**

Guidelines [71]

Key Resources

Resources:

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

  These nine pages report on a meeting that 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.

- ### Next Steps for Tenofovir Gel: CONRAD and TIA Sign License Agreement

  This press release outlines the terms of an agreement between CONRAD and the South African Government’s Technology Innovation Agency (TIA) to make 1% tenofovir gel affordable and accessible in Africa.

- ### FDA and CONRAD Chart U.S. Regulatory Path for 1% Tenofovir Gel for HIV Prevention

  The outcomes of a collaborative meeting held with key stakeholders to help clarify the next steps required for testing and licensure of 1% tenofovir gel are summarized in this press release. The U.S. Food and Drug Administration agreed that the current preclinical program for 1% tenofovir gel is sufficient to support a future new drug application and has granted Fast Track approval designation, while identifying remaining safety and quality issues to be addressed.

Guidelines

Resources:

- ### Update to Interim Guidance for Preexposure Prophylaxis (PrEP) for the Prevention of HIV Infection: PrEP for Injecting Drug Users

  After the release of the results [51] of a PrEP trial among injecting drug users in Thailand, the Centers for Disease Control and Prevention updated its interim guidance for health care providers in the United States, recommending that the preferred PrEP regimen for this

population be a combination of tenofovir disoproxil fumarate and emtricitabine.

- ## FDA Approves First Drug for Reducing the Risk of Sexually Acquired HIV Infection

  This press release announces that the U.S. Food and Drug Administration has approved the use of Truvada (emtricitabine/tenofovir disoproxil fumarate) to reduce the risk of HIV infection in uninfected men and women who are at high risk of HIV infection and who may engage in sexual activity with HIV-infected partners. It also describes a risk evaluation and mitigation strategy (REMS) to minimize the risk that people using Truvada for pre-exposure prophylaxis will become infected with HIV and to reduce the development of drug resistance. Links to additional information are provided.

- ## Guidance on Oral Pre-exposure Prophylaxis (PrEP) for Serodiscordant Couples, Men and Transgender Women Who Have Sex with Men at High Risk of HIV: Recommendations for Use in the Context of Demonstration Projects

  Noting the need for experience with pre-exposure prophylaxis outside the controlled context of a clinical trial, the World Health Organization provides guidance on the daily use of antiretroviral drugs for HIV prevention by uninfected individuals participating in demonstration projects.

- ## Southern African Guidelines for the Safe Use of Pre-Exposure Prophylaxis in Men Who Have Sex with Men Who Are at Risk for HIV Infection

  These guidelines explain what pre-exposure prophylaxis (PrEP) is, provide current 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.

- ## Truvada for a Pre-exposure Prophylaxis (PrEP) Indication: Risk Evaluation and Mitigation Strategy

  This website provides important prescribing considerations and resources for health care providers and HIV-negative individuals to ensure that Truvada is prescribed and used safely as pre-exposure prophylaxis. It is part of a risk evaluation and mitigation strategy (REMS), which is a strategy to manage known or potential serious risks associated with a drug product. This is a type of strategy required by the U.S. Food and Drug Administration to ensure that the benefits of a drug outweigh its risks.

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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.

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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.

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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.

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Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV Infection in Men Who Have Sex with Men

Interim guidance for health care providers in the United States is provided based on the results of iPrex, a large clinical trial testing the efficacy and safety of pre-exposure prophylaxis for reducing HIV acquisition by men who have sex with men. The document is intended to guide clinical practice until comprehensive U.S. Public Health Service guidelines are available.

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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.

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Interim Guidance for Clinicians Considering the Use of

Preexposure Prophylaxis for the Prevention of HIV Infection in Heterosexually Active Adults

This interim guidance for health care providers in the United States includes consideration of the results of trials of pre-exposure prophylaxis (PrEP) among heterosexual women and men, as well as the U.S. Food and Drug Administration's approval of the use of Truvada as PrEP by men and women at high risk of HIV infection. The guidance also addresses pregnancy and safety issues that were not discussed in the previous interim guidance for the use of PrEP in men who have sex with men (see below).

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 **[72]**

Communication [73]

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:

- ### An Action Agenda to End AIDS

  In a joint report, AVAC and amFAR outline a plan for beginning to end HIV/AIDS. It includes clear, time-bound targets for outcomes, as well as the responsibilities of different stakeholders to achieve these targets.

- ### Investing to End the AIDS Epidemic: A New Era for HIV Prevention Research and Development

  This document reports on investments in HIV therapeutic and prophylactic vaccines, microbicides, adult male circumcision, the female condom, pre-exposure prophylaxis, the prevention of herpes simplex virus type 2, prevention of vertical transmission, cure research, and treatment as prevention through 2011. Published every year since 2004, these reports are intended to help researchers, advocates, and donors understand and evaluate the global response to the HIV/AIDS pandemic.

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

  This is a 29-page report of 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.

- ### 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 recent situations in which a data safety monitoring board has made a recommendation that affected the conduct of a trial are reviewed.

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AVAC Report 2011: The End?

This web page provides links to a 48-page report (and individual sections of the report) from AVAC outlining a three-part, science-based agenda to end the AIDS epidemic. The agenda consists of these priorities: deliver today's proven strategies at scale for immediate impact; demonstrate and roll out newly available HIV prevention tools, including pre-exposure prophylaxis and microbicides, for even greater impact in five to ten years; and develop long-term solutions — including an effective vaccine and a cure — that will make it possible to "close the door on AIDS."

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Giving Women Power Over AIDS

The International Partnership for Microbicides provides a brief introduction to the unequal impact of the HIV/AIDS epidemic on women, the promise of microbicides as a woman-controlled method, and the essential role microbicides could play in achieving the United Nation's Millennium Development Goals.

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Advancing the Science in a Time of Fiscal Restraint: Funding for HIV Prevention Technologies in 2009

This 36-page report provides an overview of 2009 public-sector, philanthropic, and commercial funding toward research and development for HIV-preventive vaccines, microbicides, pre-exposure prophylaxis using antiretroviral drugs, and operations research related to male circumcision. The report concludes that although funding for HIV prevention has been stable during the global recession, this positive news masks some concerns about funding for HIV prevention, including the implications of level or "flat" funding.

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Anticipating Results of ARV-based HIV Prevention Trials

This 10-page document provides advocates with a "big picture" of the antiretroviral (ARV)-based prevention landscape, with a focus on trials in HIV-negative people. It covers the decisions and processes that might be triggered by data from individual trials of pre-exposure prophylaxis and ARV-based microbicides, and it describes how these trials fit together. There is also ongoing exploration of how ARV drugs could be used by HIV-positive people to reduce their infectiousness.

- ## From Promise to Product: Advancing Rectal Microbicide Research and Advocacy

  From Promise to Product features recommendations on how to advance rectal microbicide research and advocacy. Global challenges to preventing HIV during sexual intercourse and the state of rectal microbicide research are also highlighted.

- ## Gender Equality in AIDS Prevention

  Data are presented to support three key observations about the special needs and vulnerabilities of women that must be considered when addressing HIV prevention strategies: HIV/AIDS is rapidly becoming a women's epidemic in high-prevalence areas, women are biologically more vulnerable to infection and its consequences, and gender inequities prevent many women from being able to protect themselves.

- ## HIV/AIDS and the Millennium Development Goals: Microbicides and the Need for Long-Term Prevention

  Despite the availability of multiple HIV prevention options, women continue to be disproportionally affected by HIV throughout the world. This short document emphasizes the urgent need for HIV prevention options that women can control. It also discusses how microbicides could help meet the United Nation's Millennium Development Goals by 2015.

- ## Understanding the Results of CAPRISA 004

  The design of the CAPRISA 004 microbicide trial is presented in this 10-page document, including purpose, design, dosing strategy, study size and population, and trial implementers/funders. Answers are given to key questions about the trial, including: What are CAPRISA 004 data on HIV prevention? What are CAPRISA 004 data on the prevention of herpes simplex virus type 2? What happens next?

- ## The First 55 Steps: A Report of the Microbicide Development Strategy's Civil Society Working Group

  This 39-page report discusses the engagement of civil society in each phase of microbicide research, development, and introduction. It identifies the resources and 55 action steps needed to move from a minimal level of engagement to having civil society engaged as a full partner.

- ## Mobilization for Community Involvement in Microbicide Trials: Report from a Dialogue in Southern Africa

Some of the challenges and strategies discussed during a Dialogue on Community Involvement in Microbicide Clinical Trials, which was held in Johannesburg, South Africa, in July 2003, are described in this 48-page meeting report. The teams from eight trial sites in four southern African countries met to discuss challenges, share strategies, and identify opportunities for community involvement in microbicide trials.

Fact Sheets

Resources:

- ## Women and the Need for Microbicides

  The urgent need for woman-initiated HIV prevention options and how such options could complement other prevention approaches are discussed in this fact sheet.

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

  This report 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. Additional discussion in the report relates to the safety of rectal microbicides.

- ## Youth Advocates for Microbicides

  Calling for increased youth involvement in microbicides advocacy, this fact sheet identifies six critical issues for youth advocacy.

- ## Microbicides: Take Action

  This fact sheet provides an overview about microbicides, including their potential for putting the power of HIV prevention directly in women's hands and current impediments to women's access to this power. Eight actions that individuals or organizations can take to help make microbicides a reality are presented.

Films

Resources:

- ## The Rectal Revolution is Here

  “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.

- ## Hope Against HIV: Microbicide Trials in Your Community

  This video answers commonly asked questions about microbicides and the clinical trials that take place in Africa and across the globe: What are microbicides? What is a clinical trial? When will we have a microbicide? The video is viewable as a teaser (100 seconds, English) or full length (approximately 20 minutes).

- ## In Women’s Hands

  Through powerful personal stories, this film articulates the potential role of microbicides and the importance of public- and private-sector leadership, as well as citizen involvement, in this issue. The film is available in both DVD and VHS (both PAL and NTSC). All DVDs and VHS cassettes include both 10- and 25-minute versions.

Toolkits

Resources:

- ## Global Lube Access Mobilisation

  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 Mobilisation 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:

- ## 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.

- ## 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 how to organize a successful forum on microbicides.

- ## Advocates’ Guide to Statistical Terms

  This document provides an explanation of some statistical terms used to describe results in clinical trials, with an advocacy take-home message that no matter what the headlines say, a single number is not the full result.

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:

- ## ‘‘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.

- ## Communications Handbook for Clinical Trials

  Using case studies and practical insights culled from communications experience in clinical trials from around the world, this 280-page 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.

- ## Managing Expectations Around Microbicides

  This fact sheet contains several key messages that can be used to express clear, realistic expectations about microbicides in advocacy and outreach. The messages address the timing of microbicide availability, drug development, the nature of clinical trials, the likely effectiveness of microbicides, the potential cost of a microbicide, attributes of a microbicide, and resource needs of the field.

- ## Microbicide Messaging: Themes to Emphasize and Avoid

  The Global Campaign for Microbicides identifies and discusses seven key points to pay attention to when developing presentations about microbicides.

Training

Microbicide trials routinely provide training to members of the local community and to members of a community advisory board — often formed specifically for a clinical 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:

- ## Good Participatory Practice Guidelines and Tools

  This web page provides links to good participatory practice (GPP) guidelines and tools for biomedical HIV prevention trials. Links to a comprehensive set of companion tools to help research teams and other stakeholders understand, implement, and monitor the GPP guidelines, including a PowerPoint presentation and a GPP training curriculum, are included.

- ## Communications Handbook for Clinical Trials

Using case studies and practical insights culled from communications experience in clinical trials from around the world, this 280-page 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.

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Community Partners Training Materials

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

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Community Clinical Research Training Documents

Developed for use across HIV prevention trial networks, this trainer’s guide and training module cover the clinical research process, principles of clinical research, the role of a community advisory board, and principles of community involvement. The materials provided include an instructor’s guide and instructor’s notes, a participant guide, slides, and handouts for workshop activities.

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Hope Against HIV: Microbicide Trials in Your Community

This video answers commonly asked questions about microbicides and the clinical trials that take place in Africa and across the globe: What are microbicides? What is a clinical trial? When will we have a microbicide? The video is viewable as a teaser (100 seconds, English) or full length (approximately 20 minutes).

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Prevention Research E-Learning Center: Microbicides Essentials

Available online or via CD-ROM, this interactive multimedia course is intended to help a wide range of stakeholders answer questions about microbicides and the complexities of their development. It includes both basic and more nuanced information about microbicides. Users can receive continuing education credit for completing the course.

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Research Ethics Training Curriculum

The Research Ethics Training Curriculum, available in a Flash version or as a downloadable 444-page PDF, has been developed for an international audience of researchers and research ethics committee members who design or implement research that includes human participants or who conduct reviews of the ethical aspects of research. The training curriculum includes an overview of the main ethical principles to be considered in the development and conduct of research involving human participants; guidance to assist researchers in designing studies that are respectful of local cultures, regulations, and expectations; case studies for considering real-world examples of ethical issues; and ancillary reference documents on modern perspectives that shape the research ethics field. French, Portuguese, and Spanish versions of the first edition are available.

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

Resources:

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

  This five-minute video gives a human face to the CAPRISA 004 trial by interviewing and following one woman from the beginning of her participation in the study to her joy when hearing the results.

- ## Preventing Prevention Trial Failures: A Case Study and Lessons Learned for Future Trials from the 2004 Tenofovir Trial in Cambodia

The events leading up to the cancellation of the 2004 trial of oral tenofovir for pre-exposure prophylaxis in Cambodia are reviewed to identify lessons that can be learned from the process and consider how these problems can be avoided in future trials.

- ## Research Rashomon: Lessons from the Cameroon Pre-exposure Prophylaxis Trial Site

This 54-page report describes the complex circumstances leading up to the withdrawal of approvals for the 2004 pre-exposure prophylaxis trials in Cameroon and Cambodia, which resulted in missed opportunities to generate sufficient data to determine the efficacy of oral tenofovir in preventing HIV infection. The report urges prevention researchers to think actively and strategically about human, social, and political issues at every step of the conceptualization, design, conduct, and follow-throughs of trials.

- ## Ensuring Care Through Adequate Referrals and Community Partnerships for Women Participating in HIV Prevention Trials: Experience from the Phase III Carraguard™ Trial in Isipingo, Kwazulu Natal, Durban, South Africa

The South African Medical Research Council describes the strategies used to make enhanced standard of care options available to women screened out due to HIV and seroconversion or pregnancy post-enrollment in the Phase III Carraguard trial conducted in Isipingo, KwaZulu Natal, South Africa. Methodology, results, and conclusions are presented.

- ## Establishing the Standard of Care in HIV Prevention Trials: Experience of Setshaba Research Centre

The experience of the Setshaba Research Centre with a Phase III Carraguard trial completed in 2007 is presented. This slide presentation outlines the standard of care for all participants, those who were HIV-positive, and those who seroconverted. It also identifies lessons learned along the way.

Implementation Research

Resources:

- ## Identifying Optimal Strategies for Microbicide Distribution in India and South Africa: Modelling and Cost-effectiveness Analyses

This 60-page report presents the findings from a study that uses epidemiological modeling and economic analyses to explore the potential impact and cost-effectiveness of different microbicide introduction strategies in Southern India and South Africa.

Research Identifies Factors Important to Microbicide Acceptability (Pune, India)

The results of a study including 30 married women and 15 of their husbands in Pune, India, suggest that initial consideration of microbicide use depended on perceptions of the risk of HIV, microbicide effectiveness, and control of daily life events. Continued use, in contrast, depended on attitudes toward product characteristics, ability to privately insert and store products, and sexual power of users. A summary and a link to the study abstract are provided.

Source URL: http://www.k4health.org/toolkits/microbicides

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