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# **DEVELOPING DUAL COMPARTMENT MPTS THAT WORK UP FRONT AND FROM BEHIND**

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Population Council

September 9, 2015

## Multipurpose Prevention Technologies (MPTs)

- Single products designed to address multiple sexual and reproductive health needs:
  - Prevention of human immunodeficiency virus (HIV) and unintended pregnancy
  - Prevention of HIV and/or other sexually transmitted infections (STIs)
  - Prevention of HIV, other STIs and unintended pregnancy
- MPTs may deliver a single broad spectrum active pharmaceutical ingredient (API) or a combination of different APIs

## Multipurpose Prevention Technologies (MPTs)

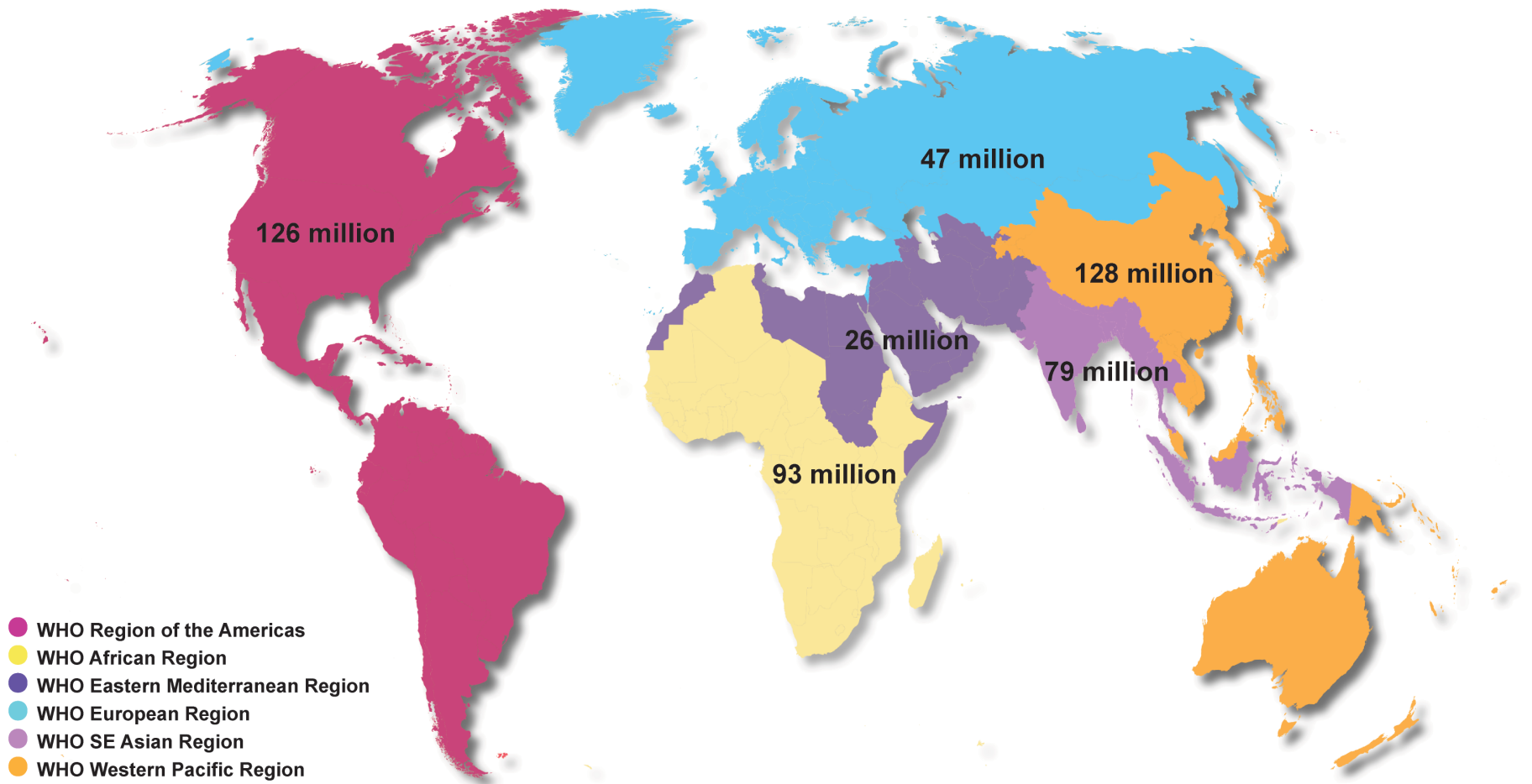
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# Curable vs Non-Curable STIs

- Curable
  - *Trichomonas vaginalis*
  - *Neisseria gonorrhoeae*
  - *Treponema pallidum*
  - *Chlamydia trachomatis*

- Non-Curable
  - *HIV*
  - *herpes simplex virus (HSV)*
  - *human papillomavirus (HPV)*

# Global Incidence of Selected Curable STIs



Modified from WHO STIs Fact sheet #110.

## What About Non-Curable Viral STIs?

- In addition to HIV and other viruses, this group includes two of the most prevalent STIs worldwide:
  - herpes simplex virus (HSV) and,
  - human papillomavirus (HPV)
- Both viruses
  - have a huge public health burden
  - are associated with increased HIV susceptibility
  - can produce vaginal and rectal infections
- Anal HSV and HPV infections are not confined to men who have sex with men (MSM)

## Herpes Simplex Virus (HSV)

- HSV-2 predominates globally (>530 million infections) but HSV-1 has emerged as the principal cause of genital disease in some areas
- Recent HSV-2 incidence in several African cohorts approximately 20 infections per 100 person-years
- MSM remain at high risk of HSV incident infection
- Treatment does not decrease susceptibility to HIV infection
- No vaccine available

## Human Papillomavirus (HPV)

- Most frequently acquired STI worldwide
- 291 million women have an HPV infection at any given time (similar number of men)
- Main cause of cervical and anal cancer
- Highly effective vaccines are available but:
  - Low uptake owing to relative high cost and distribution challenges
  - Persistent gap in coverage
  - Protection is restricted to specific HPV types

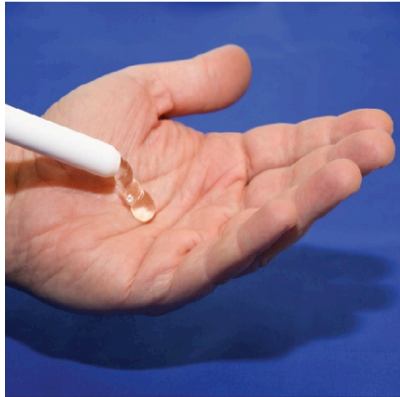


# Condoms to Prevent Vaginal and Rectal Acquisition of HIV and other STIs

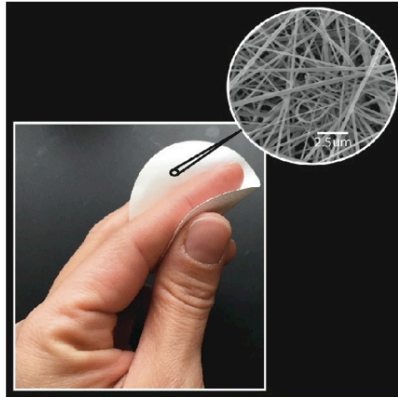


- Highly effective against most STIs as long as they are used correctly and consistently
  - HPV is an exception, condoms may not fully protect against this virus
- Increased condom accessibility and use could have a positive impact
- High risk individuals are not using them
- Other options and choices are still needed to improve sexual and reproductive health outcomes

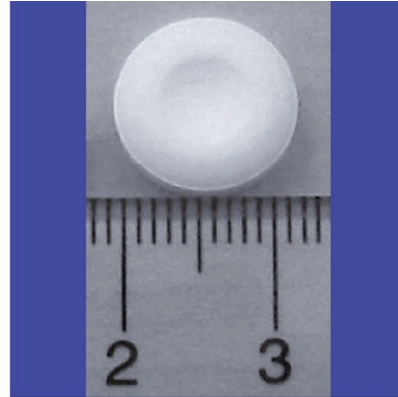
# Potential Delivery Systems for Novel Dual Compartment (Vaginal and Rectal) MPTs



Gel



Nanofiber Delivery System  
(NFDS) or Films



Fast-Dissolving Insert  
(FDI)

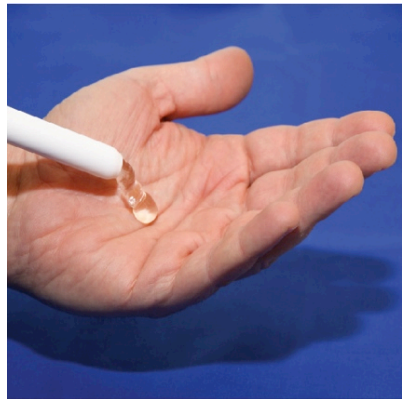


Enema or  
Vaginal Liquid Formulations

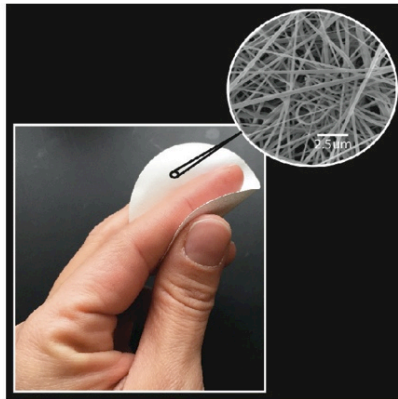


Injectable

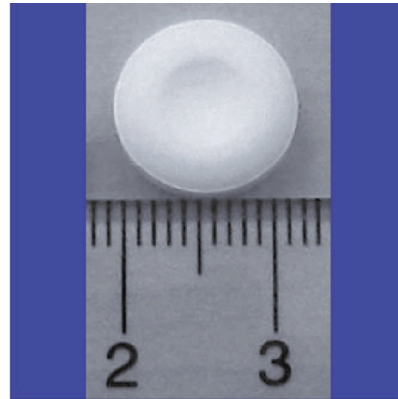
# Potential Delivery Systems for Novel Dual Compartment (Vaginal and Rectal) MPTs



Gel



Nanofiber Delivery System (NFDS) or Films



Fast-Dissolving Insert (FDI)



Enema or Vaginal Liquid formulations



Injectable

Topical Application

# Dual Compartment Topical Formulation Challenges

- Physiological and anatomical differences between vaginal and rectal compartment
  - Vagina has stratified squamous epithelium and rectum/lower gastrointestinal tract has simple columnar epithelium
  - Vaginal tract is a closed cavity while rectal compartment is longer/opened
  - Vaginal normal pH is acidic (4 - 4.5); rectum is neutral/slightly alkaline

# MPTs Targeting HIV and other STIs



SUPPORT MPTs



NEWSLETTER SIGNUP

## MPT Product Development Database

This database includes MPT products that are currently available, as well as MPT products in active development. In addition, a number of existing products and products in development for single indications are also included. The database outlines detailed product information and can be searched to display products by desired criteria as selected from the drop-down boxes or by entering a keyword in the search box. Click on the product name to access detailed information on each product. [Click here to learn more about the inclusion criteria and information update methodology.](#)

Links to **Summary Tables** outlining (1) **MPT Products in Development**, (2) **Existing Single Indication Products** or (3) **Candidate Single Indication Products** that could serve as potential components of future MPTs can be found below.

**Help us keep the database complete and up to date!**  
If you know of an MPT product not included in the database or have updated information for listed products, please contact us using the "MPT Database Feedback" form.

**MPT Database Feedback**



Check out the MPT products in the development pipeline – [view an MPT Pipeline Table by Indication Combination.](#)

Product Type <input type="button" value="Show All Product Types"/>	Delivery Route <input type="button" value="Show All Delivery Routes"/>	Delivery Method <input type="button" value="Show All Delivery Methods"/>	Development Stage <input type="button" value="Show All Stages"/>
Indication <input type="button" value="Show All Indications"/>	Product Developer <input type="button" value="Show All Developers"/>	Product Sponsor/Funding <input type="button" value="Show All Sponsors"/>	Active Ingredient <input type="button" value="Show All Active Ingredients"/>

Key Word Search

70 product(s) found

SHOW PRODUCTS

CLEAR SEARCH FIELDS

START NEW SEARCH

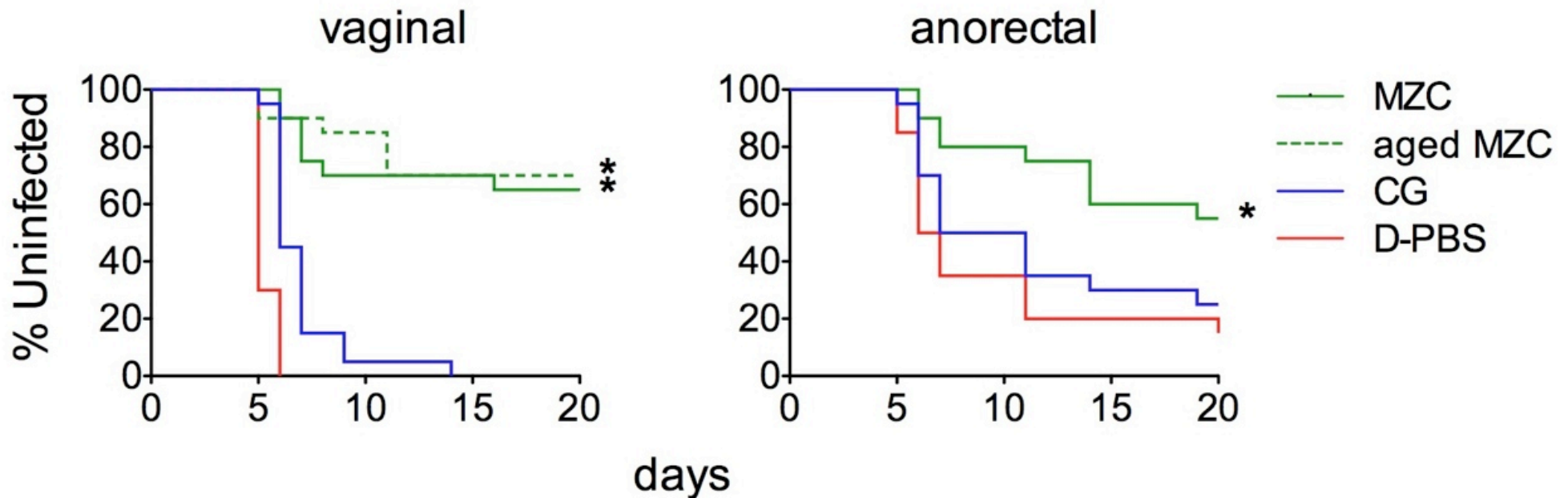
### MPT Products in Development

- ▶ [Topical - Intravaginal Rings \(IVR\)](#)
- ▶ [Topical - Gels \(Vaginal & Rectal\)](#)
- ▶ [Topical - Films \(Vaginal & Rectal\)](#)
- ▶ [Topical - Tablets \(Vaginal & Rectal\)](#)
- ▶ [Barrier Device with Drug - Diaphragms](#)

# MZC and ZC Combinations

- MIV-150 (M)
  - NNRTI; in vitro activity against a broad panel of HIV isolates/resistant viruses; *in vivo* activity vs. SHIV-RT
- Zinc acetate (Z)
  - RTI; blocks HIV and HSV-2 *in vivo*
- Carrageenan (C)
  - Attachment and entry inhibitor; blocks HPV in vitro and *in vivo*
  - Potentiates ZA's anti-HSV-2 activity *in vivo*
- Completed a Phase 1 vaginal trial of MZC (PC-1005)
- Promising data from rectal preclinical models
- ZC could be distributed over the counter (OTC)

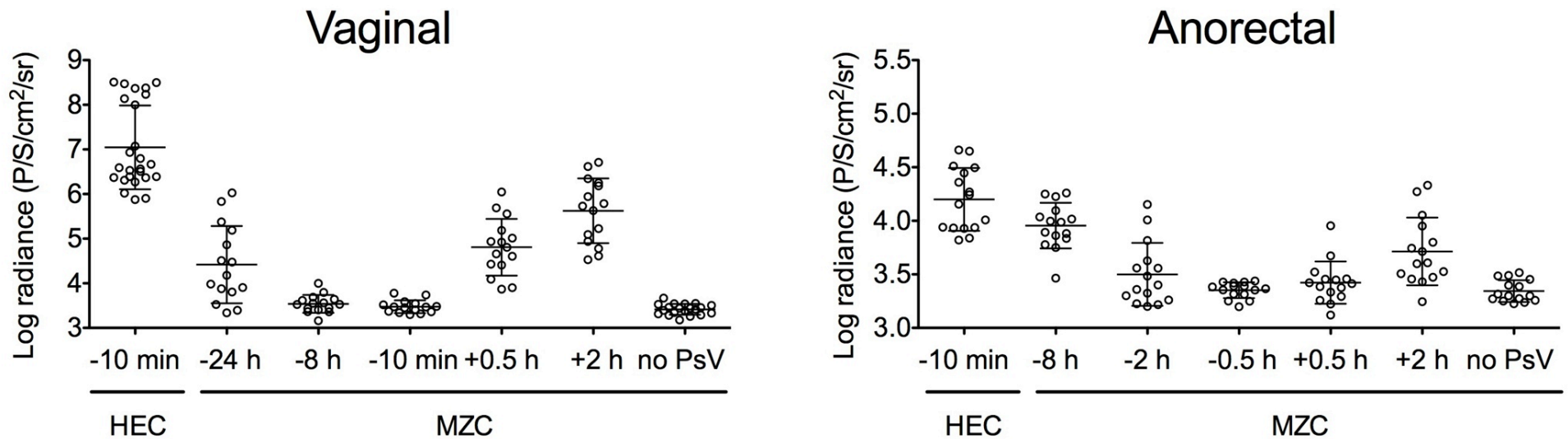
# MZC Gel Significantly Decreases HSV Infection in Mouse Vaginal and Anorectal Model



$10^6$  HSV-2 pfu per mouse (N=15),  $p < 0.05$

Kizima et al. PLoS One. 2014 Apr 16;9(4): e94547

# MZC Gel has Potent and Durable Anti-HPV Activity in Mouse Vaginal and Anorectal Models



N=15, p<0.05

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# First-in-human Trial of MZC Gel Used Vaginally: Preliminary Findings

- MZC well tolerated by women (n=22) inserting gel vaginally for up to 14 days
- Low levels of MIV-150 observed systemically; zinc plasma levels unchanged from baseline
- MIV-150 and C in CVL are active against
  - HIV and HPV in cell based-assays
  - HIV and HSV-2 in *ex vivo* explant model

## MZC or ZC Gel Status

- Pre-clinical *in vitro* and *in vivo* testing complete
- Phase 1 vaginal trial completed
- Pre-clinical rectal toxicology to be completed by end of 2015
- Candidate for MTN rectal clinical testing in 2016
- Explore possibility of ZC as OTC product

# Griffithsin/Carrageenan Combination as an MPT

- Griffithsin (GRFT)
  - Activity against HIV, HSV-2, *Trichomonas vaginalis*, HCV and HPV
  - Prevents post-adsorption steps in viral STIs
- Carrageenan (CG)
  - Attachment and entry inhibitor; blocks HPV *in vitro and in vivo*
  - Potentiates GRFT's anti-HSV-2 activity *in vitro and in vivo*
- Currently being formulated and tested at Population Council for vaginal use
  - Fast-Dissolving Inserts (FDI) have the potential for dual compartment use (collaboration with PATH and CONRAD)

# Summary

- Not just HIV
- Significant unmet need for dual compartment MPTs
- Potential delivery systems and candidates
  - MZC, ZC and GC formulations
  - CAMI website
- Funding needed for dual compartment MPTs

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# Ideas. Evidence. Impact.



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