



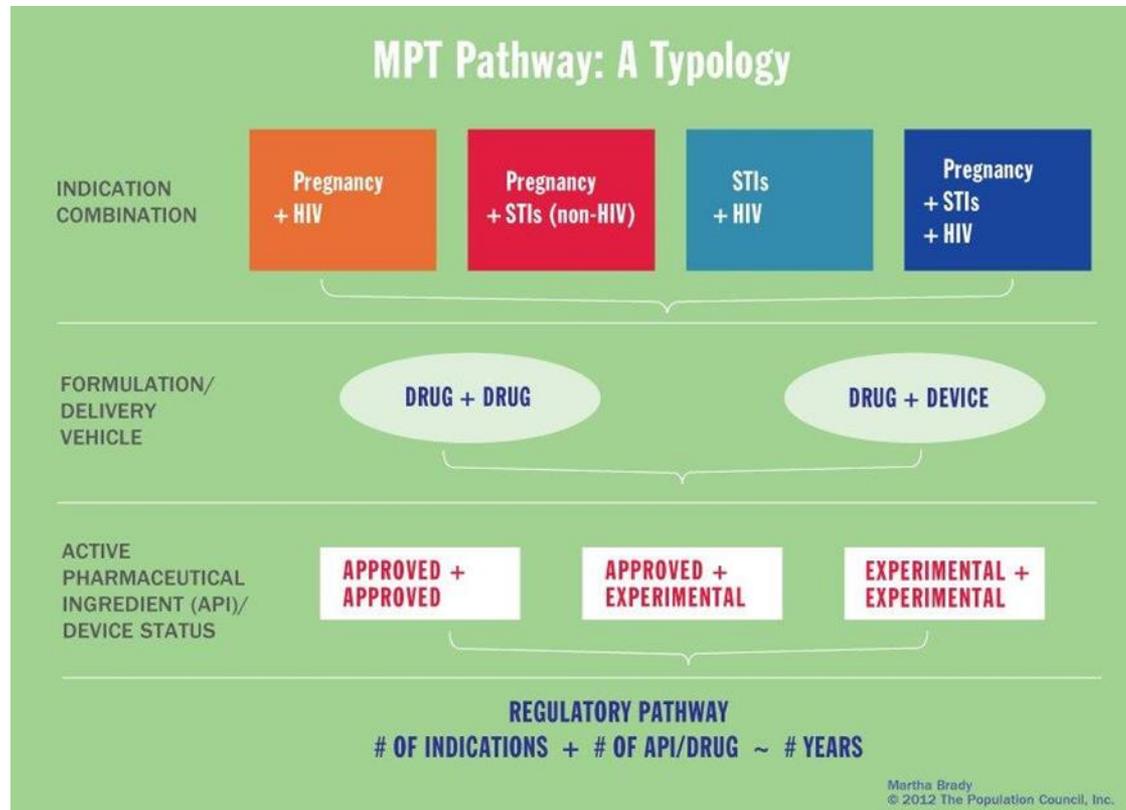
POPULATION COUNCIL'S MPT DEVELOPMENT PROGRAM

Tom Zydowsky

IMPT CT Meeting

September 14, 2016

MPT Development Overview



Brady M, Tolley E. *Aligning product development and user perspectives: social-behavioural dimensions of multipurpose prevention technologies*. BJOG 2014; 121 (Suppl. 5): 70-78

PC's MPT Strategy

- Focus on Approved + Approved or Approved + Experimental pathway initially
- Develop
 - user-initiated, on demand or sustained release (≤ 90 days) products
 - broad spectrum products with or without contraception (cMPT and MPT, respectively)
- Collaborate with external organizations to accelerate MPT development

PC's cMPT Pipeline

MPT	Indications	Development Status
MZC gel + SILCS diaphragm*	HIV, HSV, HPV and unintended pregnancy	Proposed Phase 1
MZC + HC vaginal ring	HIV, HSV, HPV and unintended pregnancy	Preclinical
Griffithsin + HC vaginal ring#	HIV and HSV and unintended pregnancy	Early preclinical

MZC = MIV-150 + zinc acetate + carrageenan (experimental)

HC = hormonal contraceptive (approved for vaginal administration)

* Collaboration with PATH

Collaboration with Oak Crest

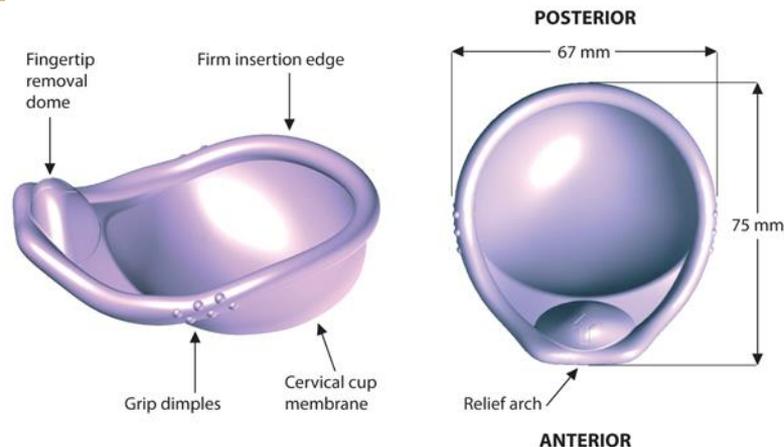
MZC Gel Overview

- MIV-150
 - NNRTI with good resistance profile
 - Active against different HIV clades and multi-drug resistant HIV
- Zinc Acetate (ZA)
 - RTI with good resistance profile
 - *In vivo* activity against SHIV-RT and HSV-2 (in a carrageenan gel)
 - Inhibits forward progressive human sperm motility and the human sperm acrosome reaction
- Carrageenan (CG)
 - Attachment and entry inhibitor; blocks HPV in vitro and *in vivo*
 - Potentiates ZA's anti-HSV-2 activity *in vivo*
- MZC attributes
 - One-two-punch against HIV
 - Broad spectrum antiviral activity *in vivo*: HIV, HSV and HPV
 - Phase 1 vaginal trial finished; vaginal Phase 1B and rectal trials planned
 - Physical compatibility with SILCS diaphragm

SILCS Diaphragm: Designed to Meet User Needs



- Easy to insert
- Comfortable to wear
- Stable, confident fit
- Easy to remove
- Single-size device
 - Fits most women
 - No need for pelvic exam
 - Simplifies supply logistics and delivery



SILCS Commercialization Status

- SILCS technology licensed to Kessel medintim GmbH in 2010
- Regulatory approvals achieved in multiple countries, including Europe, Canada, Australia, and U.S.
- Launched first in EU countries in 2013 as Caya® contoured diaphragm; now marketed in 25+ countries
- Developed country introduction used to build experience and raise awareness and interest in developing countries
- CayaGel (a CE mark certified contraceptive gel containing lactic acid) marketed for use with the Caya® contoured diaphragm
- MZC gel proposed to replace Caya Gel

TPP for MZC Gel + SILCS

Attribute	Target
Duration of protection	8 hours
Number of pregnancies expected (per 100 women-years)	18 for typical use; 14 for perfect use
Antiviral efficacy	HIV: 70% HSV: 60% HPV: 90%
API amounts in 4 gram of MZC gel	MIV-150: 0.07 mg zinc acetate: 3 mg carrageenan: 30 mg
Gel storage conditions and shelf-life	Stable for 30 months at 30°C/65% RH, and 18 months at 40°C/75% RH.
Cost of MZC gel (per 4 gram dose)	<\$0.10

Value Proposition: Gel + SILCS

- Alternative delivery system with added value
 - Comparable to vaginal applicators for delivery of gels
 - Reusable for 2 years = reduced cost for packaging and delivery
 - Less environmental impact due to reuse of delivery system
 - Holds gel high in the vagina = less messiness and gel leakage
- Potentially less stigma by associating product with contraception
 - FP methods are generally accepted by couples; less stigma than use of a product for HIV prevention alone
- cMPT: Broad spectrum HIV/STI protection + contraception
 - Women more interested in a product that offers dual protection

SILCS Diaphragm as an MPT

- **Objective:** Assess acceptability and preference for the SILCS for microbicide gel delivery compared to gel delivery from a prefilled applicator
- **Method:** 106 South African women used each method during five separate sex acts
- **Results:**
 - 83% of women felt comfortable with SILCS
 - 68% interested in using SILCS + gel if it could protect from both unintended pregnancy and HIV
 - 18% interested in SILCS for pregnancy protection
 - 14% interested in microbicide gel for HIV prevention

Beksinska, Smit, Maphumulo, et. al. Poster at ESC Congress, April 2016

Draft Clinical Plan for MZC Gel + SILCS

Study	Status
<u>MZC Gel Only</u> : 14 day Phase 1 vaginal safety	Completed
<u>MZC Gel Only</u> : 28 day Phase 1 B expanded vaginal safety with male tolerance/penile safety	Proposed (STAR STI CTG)
<u>MZC Gel + SILCS</u> : Post-coital Testing (PCT) Randomized X-over of SILCS + 4ml MZC gel, K-Y or N-9	Proposed
<u>MZC Gel + SILCS</u> : 3-6 month Phase 2B - 1° Contraception - 2° HIV prevention (HSV, HPV)	Proposed
<u>MZC Gel + SILCS</u> : Two Pivotal Phase 3 safety and efficacy trials - 1° HIV prevention - 2° Contraception, HSV, HPV	Proposed

Risks and Gaps

- Technical feasibility
 - Contraceptive/HIV/STI efficacy of MZC gel
- Strategic
 - Unknown role within overall contraceptive and MPT method mix
 - Market analysis
 - Acceptability, interest and uptake
 - Cost effectiveness/health impact modeling
 - Potentially complex regulatory pathway for a cMPT

Summary

- The SILCS diaphragm is an approved contraceptive, with a demonstrated consumer interest, and growing markets.
- SA women are more interested in a Gel + SILCS cMPT compared to a diaphragm or gel alone.
- MZC is active against HIV, HSV and HPV, (and sperm?) and completed Phase 1 vaginal trial.
- MZC + SILCS could help meet the SRH needs of women in developing countries.

Acknowledgments



Frederick



Donors



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