



Symposium 6: Prevention of Multiple Reproductive Health Indications

**High-impact products: Necessary attributes,
development prospects, and challenges**

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March 6, 2012



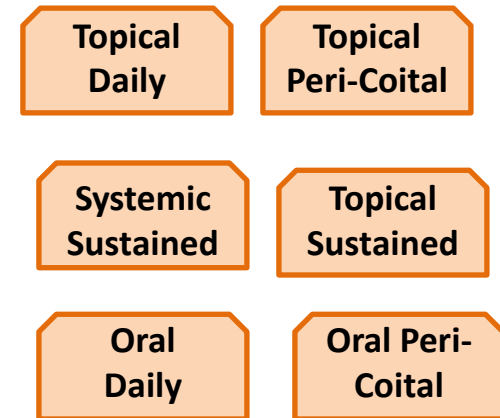
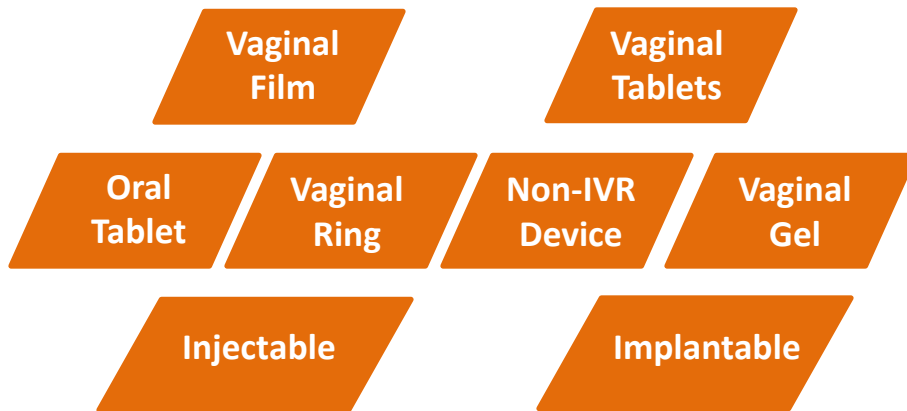
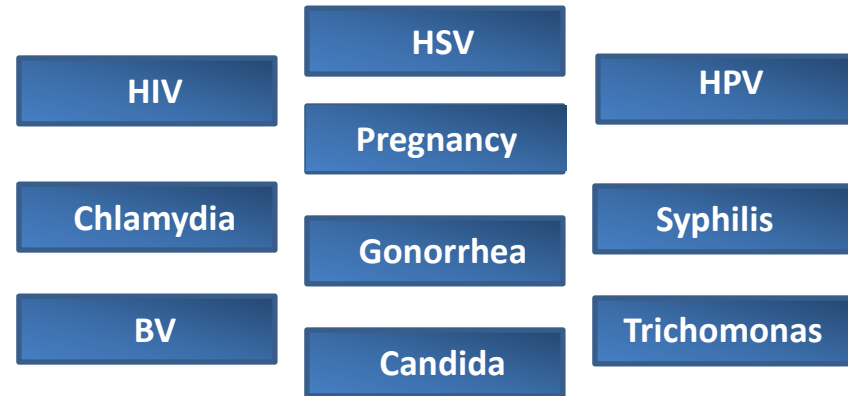
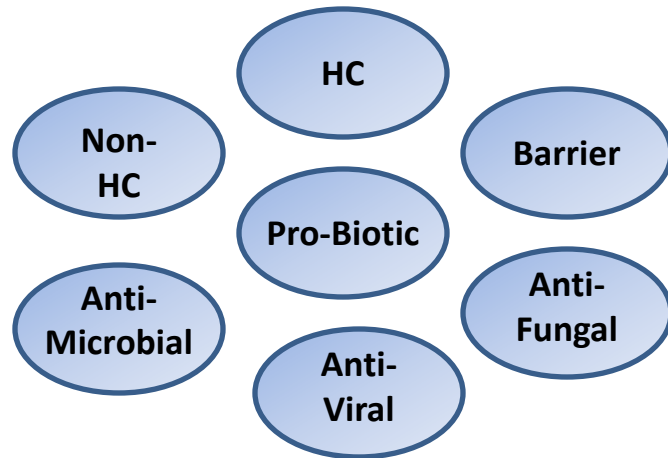
Part 1: Necessary Attributes and Parameters

Sexual and Reproductive Health Multi-purpose Prevention Technologies

- Type 1: Drug:Drug or Drug:Device
 - API(s) for at least two SRH indications in a single dosage form
 - E.g., TFV gel for prevention of HIV and HSV
 - API(s) in a device configuration for at least two SRH indications
 - E.g., Diaphragm releasing TFV
- Type 2: Multi-Indication Vaccine
 - Single product, multiple indication vaccine
 - E.g., Single vaccine preventing HSV and HPV



MPT Products: Wide Array of Possibilities



Focus and Prioritization Required

Necessary Attributes & Parameters: Target Product Profile

- May 5, 2011 Think Tank
 - USAID, CAMI, AVAC
- Think Tank Description of a TPP:
 - How a proposed candidate product addresses critical attributes
- Why a TPP?
 - To define attributes/parameters for MPT products with highest potential public health impact (i.e., prioritization)
 - To Guide donor investment and sponsor development strategies
- Two working groups formed
 - Drug-Drug/Drug-Device
 - Vaccines

Necessary Attributes:

Target Product Profile WG Results

- **Indications:**
 - HIV & Pregnancy
 - HIV & STI
 - HSV, HPV, BV
 - STI & Pregnancy
- **Dosage Forms:**
 - Sustained release
 - Topical over oral
 - Peri-coital over daily
- **Product Related:**
 - 40°C storage
 - 36 month shelf life
 - Concealable presentation

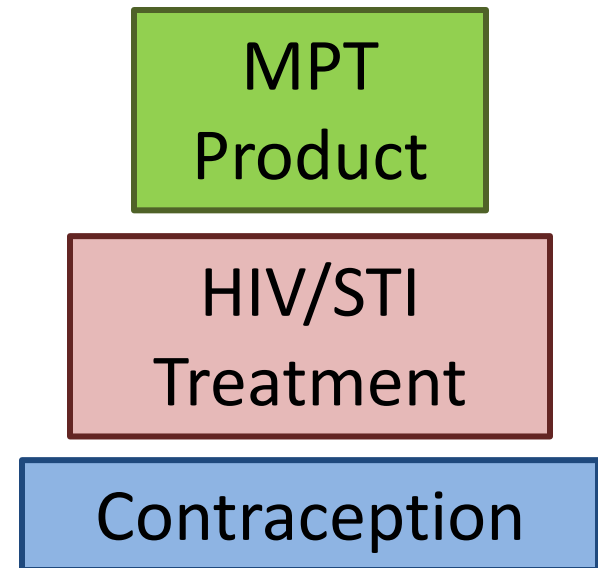
Critical Attribute	Critical Attribute
Indications	Adherence
Target Population	Time to Market
Administration Route	R&D Costs
Product Presentation	Reversibility
Dosage Form & Schedule	Side Effects
Efficacy	IP Status
Storage Conditions	Access Potential
Shelf Life	Other Health Benefits
Cost	Contra-indications, warnings, precautions, use by preg/lact women
Packaging	
Disposal/Waste	



Part 2: Development Prospects

MPT Concept Viability: Building Blocks

- Contraceptive products exist in multiple configurations
- Drugs for treatment of HIV and STI are available
- Infectious disease prophylaxis established
- Prevention of HIV:
 - PMTCT
 - Caprisa 004
 - iPrEx
 - Partners PrEP
- Individual and multi-purpose vaccines: MMR, DPT



Early to Later Stage MPT Product Candidates: HIV and Pregnancy

	Discovery	Development		Developing world registration / Launch
Dual protection	<ul style="list-style-type: none"> Bioengineered Lactobacillus PC6-inhibitor Dendrimer gels Rehydrating foam 	<ul style="list-style-type: none"> Praneem tablet (P2) Duet+TFV gel (P1) SILCS+TFV gel (PC) TFV+LNG ring (PC) 	<ul style="list-style-type: none"> DPV+LNG ring (PC) DPV+(P+E) ring (PC) MIV-150+LNG ring (PC) 	<ul style="list-style-type: none"> Male condom (L) Female condom (L)
HIV prevention ¹	<ul style="list-style-type: none"> Bioengineered Lactobacillus Glycerol monolaurate CCR5/GP 120/inhibs GP 41 inhibs 	<ul style="list-style-type: none"> DPV ring (P3) TDF and TDF/FTC oral (P2) VivaGel (P2) 	<ul style="list-style-type: none"> TMC278 LA (P1) Maraviroc+DPV gel (PC) TFV ring (PC) MIV-150 ring (PC) 	<ul style="list-style-type: none"> TFV gel (P2/R)²
Contraception	<ul style="list-style-type: none"> Bioengineered Lactobacillus LIF and IL-11 SGK-1/AKT 	<ul style="list-style-type: none"> P-only oral (pericoital) (P3) C31G gel (P3) BufferGel (P3) 	<ul style="list-style-type: none"> Ulipristal vaginal ring (P2) LNG butanoate (P1) LNG gel (P1) 	<ul style="list-style-type: none"> P-only injectable (L) P+E oral (L) P-only ring (L) P+E injectable (L) P+E ring (R) Depo-SubQ (R)

PC = Pre-clinical; P2 = Phase II; R = Regulatory; P1 = Phase I; P3 = Phase III ; L = Launched

Note: DPV = Dapivirine, TFV = Tenofovir, TDF = Tenofovir disoproxil fumarate, FTC = Emtricitabine, LNG = Levonorgestrel, P-only = progestin-only, P+E = progestin + estrogen
 Source: USAID-sponsored CAMI MPT Product Mapping; expert interviews; BCG research

Dual Protection Concepts Closest to Potential Launch: HIV & Pregnancy

First generation new DP
(launch by ~2020)

Next generations of new DP
(launch likely beyond ~2020)

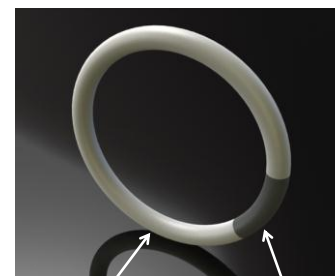
		First generation new DP (launch by ~2020)	Next generations of new DP (launch likely beyond ~2020)
Continuous use	Systemic HIV Px	<ul style="list-style-type: none"> Injectable: ARV + HC Oral: ARV + HC 	<ul style="list-style-type: none"> Implant that releases ARV and HC IUD that releases ARV Injectable passive immunization + HC
	Topical HIV Px	<ul style="list-style-type: none"> Vaginal ring: ARV + HC 	<ul style="list-style-type: none"> ARV gel + HC gel Lactobacillus (HIV Px + contraception)
Pericoital use	Systemic HIV Px		<ul style="list-style-type: none"> Oral ARV + oral HC
	Topical HIV Px	<ul style="list-style-type: none"> Cervical barrier + ARV gel Gel: ARV gel + HC gel Female condom + ARV gel 	<ul style="list-style-type: none"> ARV tablet/film + HC tablet/film Non-ARV-based dual protection gel/foam

MPT Candidate: TNF-LNG IVR for Pregnancy, HIV, and HSV

C | O | N | R | A | D
 Leaders in Reproductive Health and HIV Prevention

- **90 Day TNF/LNG IVR:**

- Segmented configuration
- Different PU and architecture for controlled delivery of 2 API
- Manufacturing via component fabrication and assembly
- TFV release in sheep
- LNG release in rabbits



TNF

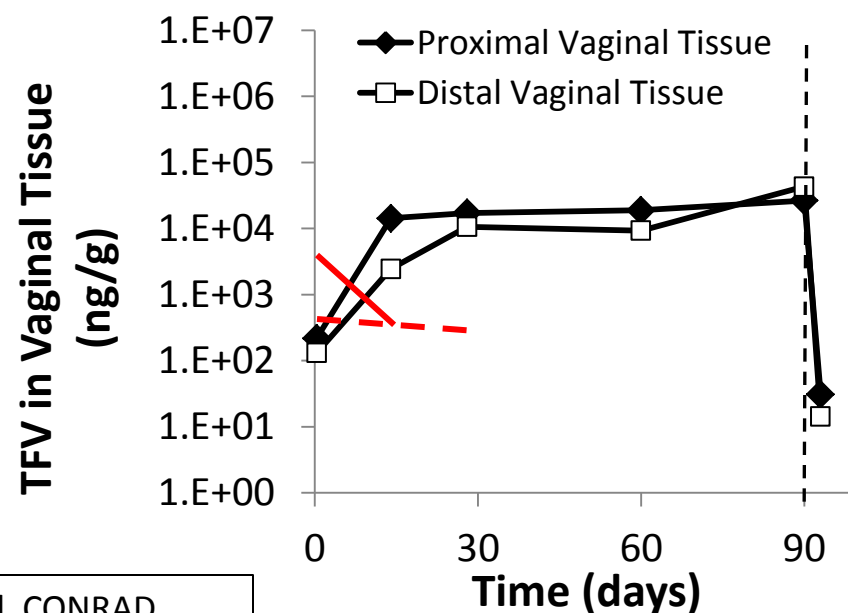
LNG

1.0% TNF Gel

--- Distal Tissue

— Proximal Tissue

TFV IVR in Sheep



MPT Candidate: MIV-150, Zn-Acetate, Carrageenan Gel

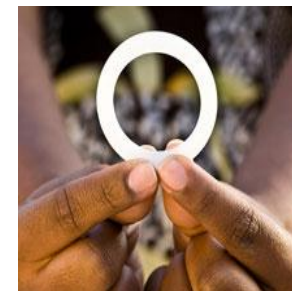


- **Indications:**
 - HIV, HSV, HPV(?) prevention
- MIV-150/ZA/CG
 - 50 μ M MIV-150 (NNRTI), 14 mM Zn-acetate in carrageenan
 - Safe in initial preclinical studies
 - Stable: 9 mos, 30°C, 65% RH; 6 mos, 40°C, 75% RH
 - Activity:
 - Protects in NHP/SHIV-RT model 24 hr post dose
 - Prevents vaginal and rectal HSV-2 infection in mice (high dose challenge)
 - Phase 1 clinical studies planned for Q3-Q4 2012

Pre-Clinical MPT Candidate Products: Funded by USAID



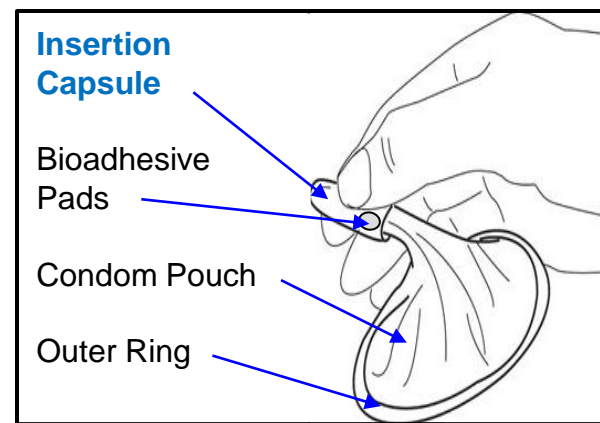
- 60 Day Dapivirine + HC IVR (IPM)
 - HIV and Pregnancy Prevention
- MZL Peri-coital Gel (Population Council)
 - HIV, STI, Pregnancy prevention
- 30 Day MZL IVR (Population Council)
 - HIV/STI/Pregnancy prevention



MPT Candidate Drug Device Combination: Drug + Barrier



- SILCS Diaphragm + 1.0% TFV Gel (PATH, CONRAD, NICHD)
 - Barrier contraception via SILCS
 - HIV/HSV prevention via TFV gel
- Female condom + Microbicide film (PATH, CONRAD, NICHD)
 - EU CE Mark received 12/10
 - WHO prequalification underway
 - U.S. contraceptive ongoing
 - Fast dissolving film delivers ARV to upper vagina and cervix



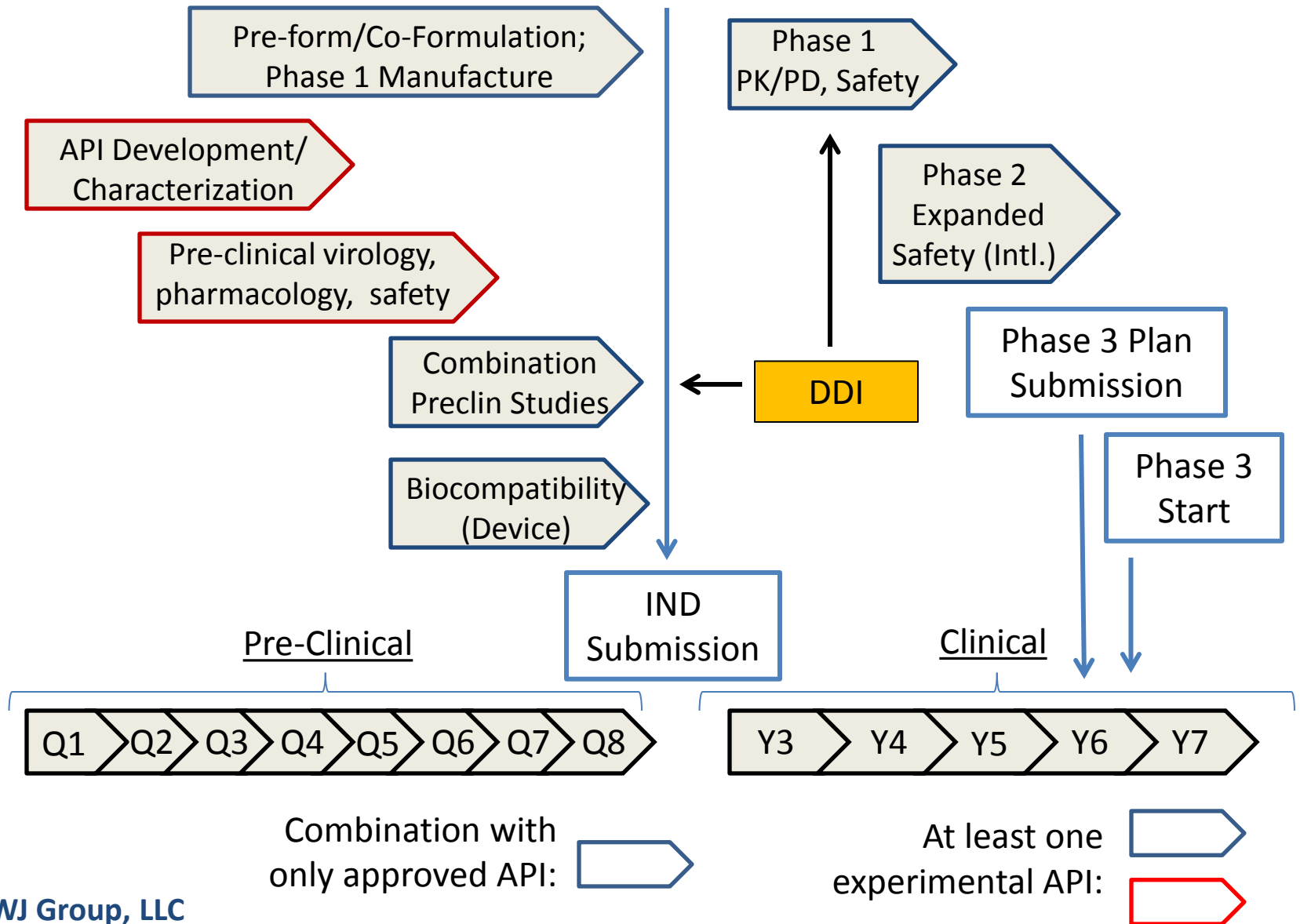
MPT Vaccine Concepts

- Work by K. Whaley, Chair of MPT Vaccine Working Group
 - Solicited MPT Vaccine Concepts
 - 11 responses
- Some Examples:
 - A. Wu; Center for Public Health Research, Nanjing University
 - HIV-1, HSV-2, HPV: Targeted induction of neutralizing Ab via synthesized peptides and ADVAX adjuvant
 - L. Stanberry, Columbia University
 - HIV-1, HSV-2, HPV: Maintain protective [cervicovaginal antibodies] and/or detectable pathogen specific T-cells; Tampon vaginal delivery of nanoemulsions of protein antigens



Part 3: Development Challenges

MPT Development & Timelines



MPT Development Challenges

- Hormonal Contraception and HIV Risk
 - Relevance to HIV + Pregnancy MPT product design and development
- Regulatory
 - May 10, 2012 FDA Scientific Advisory Meeting: Oral truvada for HIV prevention
- Resources
 - Money, trial capacity, participants, development partnerships
- **Regional MPT Needs**
 - Specific MPT priorities for different countries/regions
 - Multiple, alternative TPPs

Cost Benefit Model for MPT: HIV and Pregnancy Prevention

Scenario A: Preventing 10,000 infections in women using HIV PrEP only-

Assumptions:

3% Incidence, 50% adherence, 95% efficacy, PPY
cost of PrEP= \$150

Cost to avert 10,000 infections: **\$105M**

Scenario B: Preventing 10,000 infections in women using dual protection HIV PrEP/contraception MPT

Assumptions:

3% incidence, 60% adherence, 95% efficacy, PPY
cost for PrEP+Contraception= \$160 (+\$10)

Cost to avert 10,000 infections: **\$94M** (↓11% vs PrEP only)



Summary:

- General MPT product attributes/priorities defined
 - Regional differences
- Some MPT product development consistent with TPP is underway
 - Is it sufficient? Gap analysis needed (“Roadmap” Exercise)
- MPT product development has typical and unique challenges
 - Resolution of MPT challenges to be determined



Thank You and Questions

Acknowledgments:

D. Friend, CONRAD

J. Manning, USAID

M. Kerrigan, BMGF

K. Whaley, MAPP, Inc

IMPT Drug:Drug/Drug Device Working Group

Boston Consulting Group

Microbicides Trials Network

M. Robbiani, Population Council

M. Brady, Population Council

B. Young-Holt, CAMI/PHI

P. Harrison, CAMI/AVAC