

Multipurpose Prevention Technologies: New drugs, New Delivery Systems



Helen Rees

Southern African HIV Clinicians Society Conference, Cape Town , 2014

Executive Director, Wits Reproductive Health & HIV Institute

Personal Professor, Department of Obstetrics & Gynaecology, University of Witwatersrand

Honorary Professor, London School of Hygiene & Tropical Medicine



What is Multipurpose Technology (MPT)?

An MPT is a single product intentionally designed to prevent a combination of unintended pregnancy, HIV, and/or other STIs.



MPTs for an earlier generation

Dec. 5/15

MAGAZINE SECTION OF THE NEW YORK SUNDAY CALL

Margaret Sanger Defends Her Battle For the Right of Birth Control

Mrs. Sanger, author of the accompanying article, editor of the short-lived Woman Rebel and one of the pioneers in the general movement for allowing birth control in the United States, is at present in England carrying on her work, for she faces imprisonment if she returns to the United States and carries on the same work here. When her book, "What Every Girl Should Know," was published serially by The Sunday Call, the postal authorities endeavored to suppress it, and held up one installment several weeks. Her husband, William Sanger, recently served a jail term in New York for giving one of Mrs. Sanger's pamphlets to a collector who represented himself as a friend of the movement, but turned out to be an spy employed by the Infancy Commission. The imprisonment of Sanger brought about a national organization for repeal of the laws prohibiting the giving of birth control information. The death of the Mullinger baby in Chicago gave an impetus to this propaganda, which will be laid before Congress with a demand that the Federal censorship be abolished. Mrs. Sanger, by the way, is the mother of three children.

By MARGARET SANGER.

It is quite natural and consistent with capitalist laws that there should be a heavy penalty for imparting information on birth control among the workers, when we view these laws in the light of our present-day society.

In the South, little, pale-faced children, 9 and 10 years of age, wend their weary way to the mills early in the winter mornings, before the sun is up, and return, after twelve hours' toil, after it has set. These little ones are just "helpers" to their mothers, who work in the mills also, while the father remains at home, cares for the younger children, and takes the noonday meal to his wife and children in the mills. There are eight and nine children to a family.

Almost all the stockholders of these mills are legislators, Congressmen, etc., who have much to do in the making of the laws. So it is to their interest that child slaves be born into the world, and they will enforce the laws to that end.

When women have the knowledge of the means to avoid producing hands, when will child labor cease, and the few children born to the workers will be

made welcome by society, and given fields and playgrounds in which to spend a healthful childhood instead of grinding their souls and bodies into profits, as is done today.

A LARGE FAMILY OF CHILDREN IS ONE OF THE GREATEST OBSTACLES FOR THE WORKING MAN AND WOMAN IN OBTAINING ECONOMIC FREEDOM. IT IS THE GREATEST BURDEN TO THEM IN ALL WAYS.

It is the man with a large family who is most often the burden in a strike. It is he who is the most difficult to bring out on strike, for it is he and his wife who are the greatest sufferers through its duration.

One could enumerate various instances where two or three groups of workers have broken a strike, and upon looking for the cause you invariably found the men in these groups or nationalities had many children.



MRS. MARGARET SANGER

and could not withstand their re-
My Magazine, The Woman

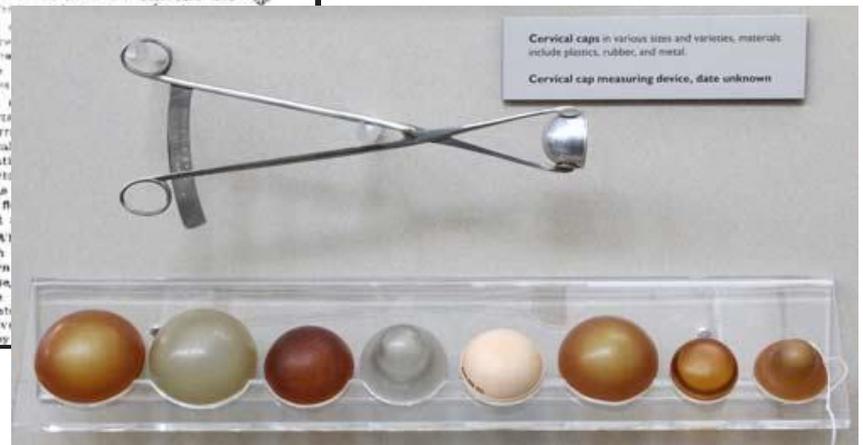
told the working women these things and more.

As editor and publisher of The Woman Rebel I felt a glow of hope and inspiration in the response which came from the working girls and women all over the United States.

I saw the women of wealth, the masters' wives, obtain birth control information with little difficulty.

I saw that, if the working man's wife refused to have more children, she was compelled to resort to abortion. Over 50,000 abortions are performed in the United States each year, and 25,000 deaths occur as the result of them.

I saw that it is the working women who fill this death list, for though the master's wife may resort to abortions, too, she is given the best care and



MPTs: Historical Precedents

H₂O + flouride

The pill + iron

Grains + folic acid



Currently Available MPTs

Male Condom



Female Condom



Diaphragm



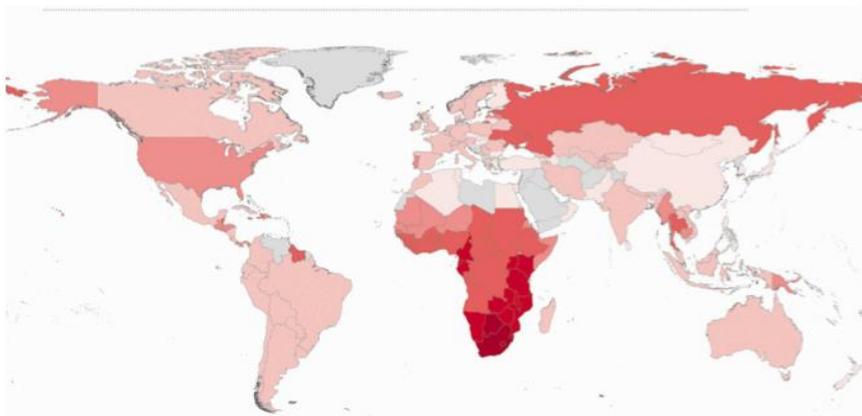
ADVANTAGES: Available now in some countries

DISADVANTAGE: Use rates are low, difficult to negotiate

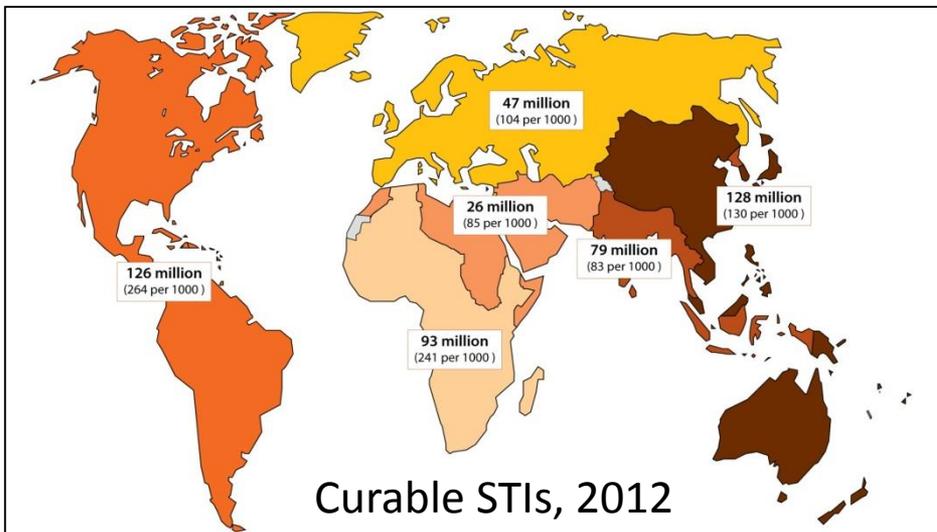
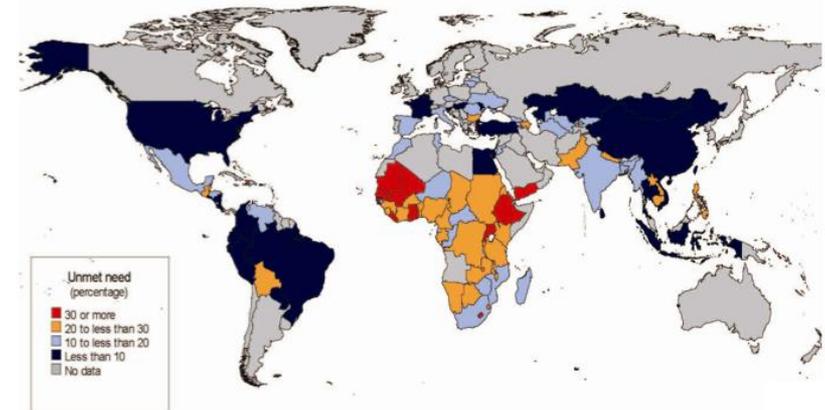


The Epidemiological argument for MPTs

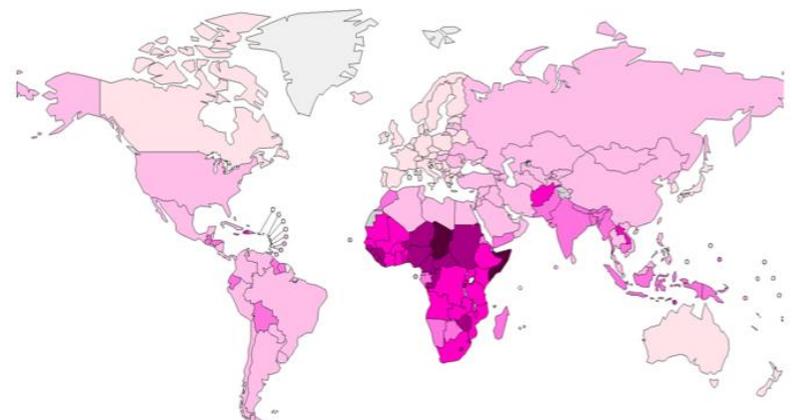
2010: A global view of HIV infection



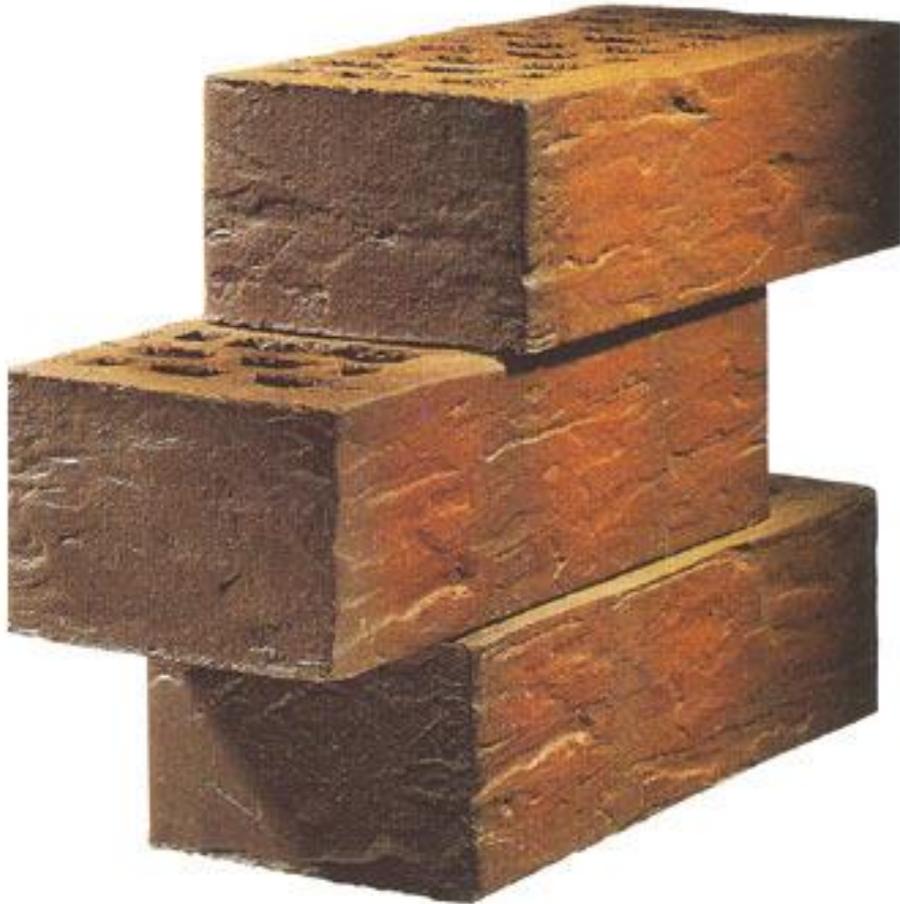
Unmet Need for Family Planning, 2011



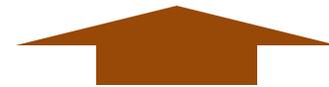
Maternal Mortality Ratio, 2010



MPT Product Profile: A simple logic



MPT PRODUCTS

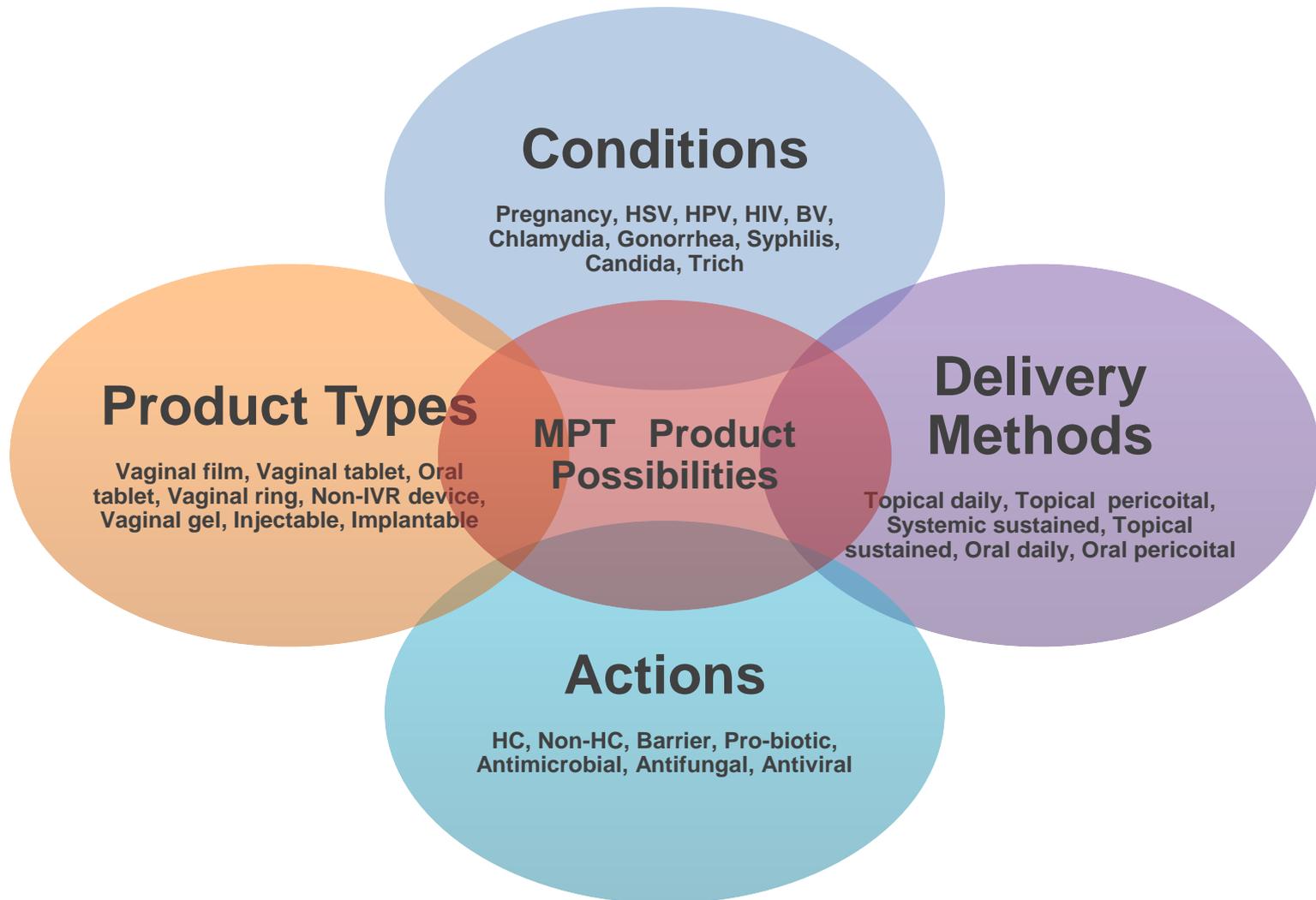


HIV/STI Prevention



Contraceptives

MPTs: Many Possibilities



Global effort to coordinate MPT development

- Greater *efficiency* in terms of cost, access and delivery of SRH prevention products
- Insufficient resources, research and finance, to develop all possibilities
- Capitalize on the demand in populations using one product type to achieve uptake and use of a second “product”



Surveys to develop Target Product Profiles (TPPs) for MPTs

- SRH researchers and product developers
- US, African and Indian providers:
 - 593 US providers, 289 African providers, 34 Indian providers
- Identify key attributes/parameters for MPT products that would lead to highest potential public health impact and guide product development and donor investment strategies

TPP Input from SRH Researchers

Critical Attributes Considered:

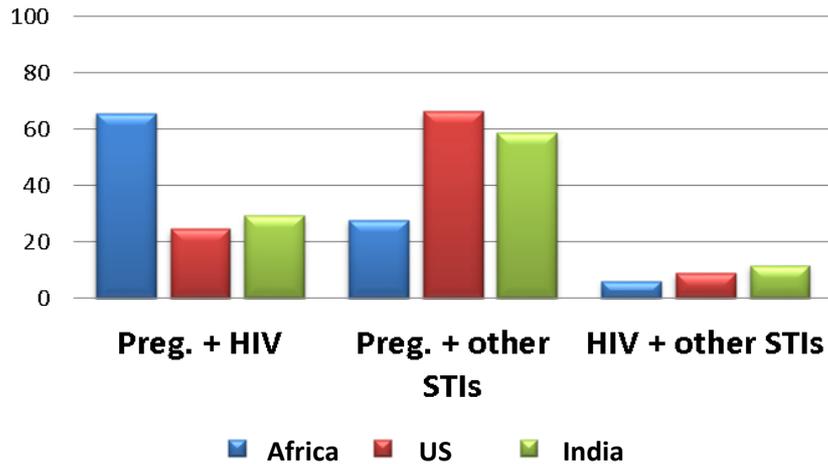
Indications	Target Population
Efficacy	Adherence
Route of Administration	Dosage Form & Schedule
Side Effects	Storage Conditions
Reversibility	Other Health Benefits
Contra-indications & precautions	Use by pregnant/lactating women
Product Provision (Rx vs. OTC vs. ?)	Access Potential & Restrictions (testing?)
IP Status	R&D Costs
Time to Market	Product Cost
Product Presentation	Packaging
Shelf Life	Disposal/Waste

Researchers Priorities:

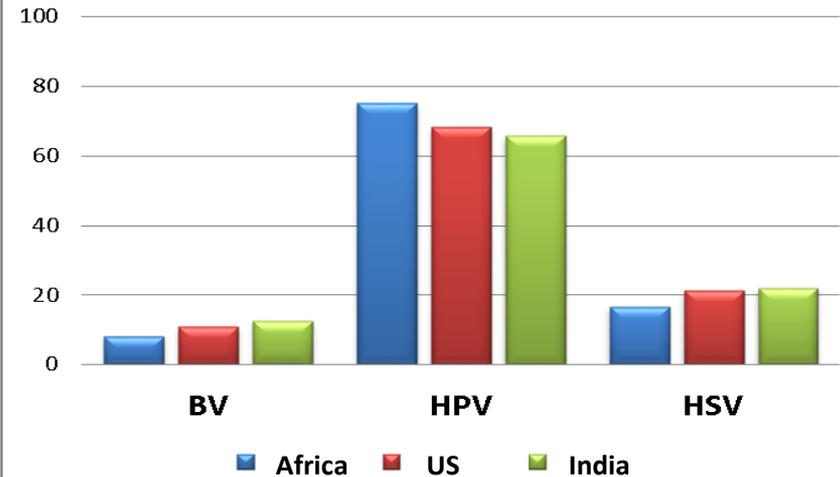
- **Indications:**
 - HIV & Pregnancy
 - HIV & STI
 - HSV, HPV, BV
 - STI & Pregnancy
- **Dosage Forms:**
 - Sustained release
 - Topical over oral
 - On demand over daily
- **Product Related (e.g.):**
 - Concealable presentation
 - 36 month shelf life
 - 40°C storage

Regional Providers' Priorities

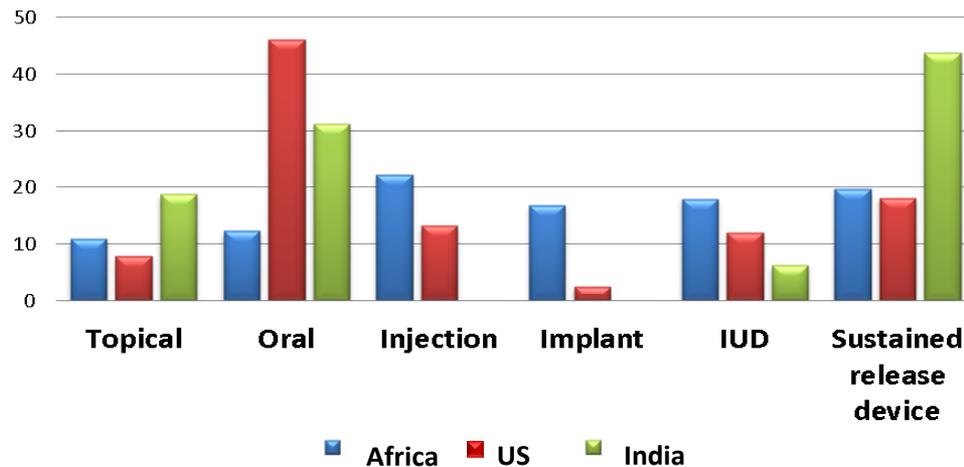
Priority Indications for MPTs



Priority STI (other than HIV)



Priority Dosage Form



Potential MPT Delivery Methods

Devices

Vaginal Rings

Vaginal Tablets

Vaginal Films



Potential MPT Delivery Methods

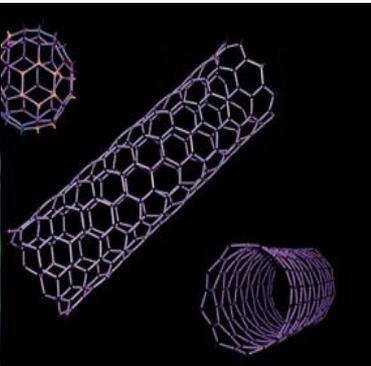
Drug combinations

Drug/device combinations

Multipurpose vaccines

Bacterial therapeutics

Nanoparticles



On-Demand Products

1% Tenofovir Gel
(FACTS 001)



- 1st Vaginal microbicide: Phase 3 South African study (FACTS 001): results 2015
- From CAPRISA 004, activity against HIV-1 (39% protective) and HSV-2 (51% protective)
- Coitally-dependent (BAT-24)

On-Demand Products

1% Tenofovir Gel (FACTS 001)



- 1st Vaginal microbicide: Phase 3 South African study (FACTS 001) results 2015
- Activity against HIV-1 (39% protective) and HSV-2 (51% protective)
- Coitally-dependent (BAT-24)

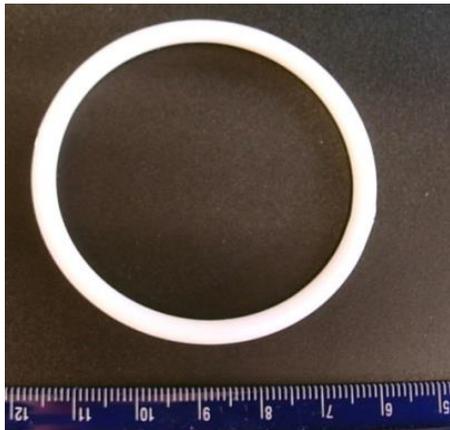
SILCS (PATH, CONRAD, NICHD)



- “One size fits most” silicone diaphragm
- Intended for OTC pregnancy prevention
- 5-year shelf life, re-use for 3 years
- Non-hormonal MPT protection: pregnancy, HIV, HSV-2 up to 24 hrs

Sustained Release Devices: Combination Intravaginal Rings

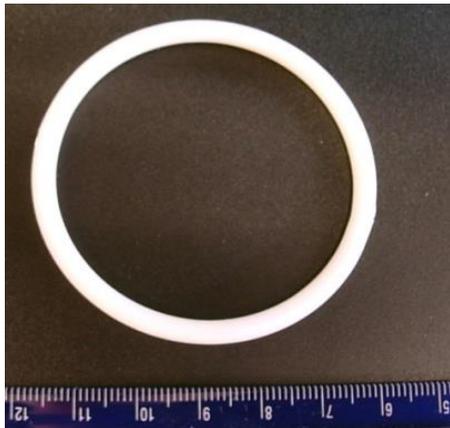
30-day MZL Combo
(Pop Council)



- MIV-150 + Zinc Acetate + LNG
- Demonstrated single-API success
- Pregnancy, HIV, HSV2, HPV

Sustained Release Devices: Combination Intravaginal Rings

30-day MZL Combo
(Pop Council)



- MIV-150 + Zinc Acetate + LNG
- Demonstrated single-API success
- Pregnancy, HIV, HSV-2

60-day Dapivirine + LNG
(IPM)



- DPV + LNG
- Testing underway, clinical studies 2013
- Pregnancy, HIV

Sustained Release Devices: Combination Intravaginal Rings

30-day MZL Combo
(Pop Council)



- MIV-150 + Zinc Acetate + LNG
- Demonstrated single-API success
- Pregnancy, HIV, HSV2

60-day Dapivirine + LNG
(IPM)



- DPV + LNG
- Testing underway, clinical studies 2013
- Pregnancy, HIV

90-day TFV + LNG
(CONRAD)



- TFV + LNG
- Testing underway, clinical studies 2013
- Pregnancy, HIV, HSV-2

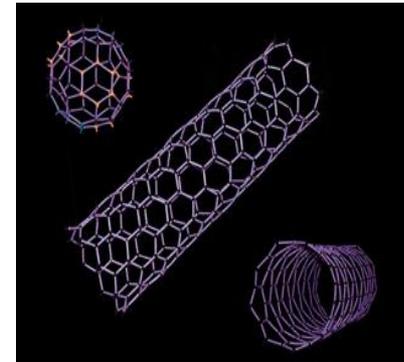
Sustained Release Devices: Combination Intravaginal Rings

Nuvaring Type MPT Technology



- Novel polymer/co-extrusion IVR
- Multiple API delivery
- Established scale-up manufacturing system

MZL Combo NFD (Pop Council)



- MIV-150 + Zinc Acetate + LNG in Nanofiber delivery system (NFD)
- Prevent pregnancy, HIV, HSV-2, HPV
- Up to 24-hrs protection
- Preclinical evaluation underway

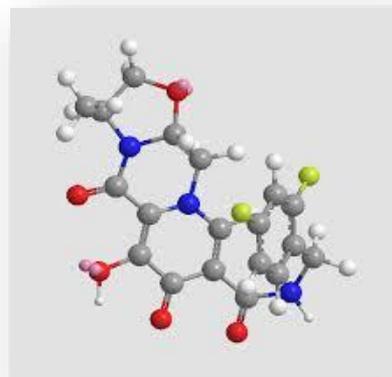
Long Acting Injectables

TMC278LA (rilpivirine; PATH)



- Injectable nano-suspension of approved NNRTI
- Long acting: 2-3 mos (?)
- Multiple trials:
 - P1 dose ranging PK; SD/MD PK/PD
 - P2 planning

GSK '744 (II; ViiV)



- Experimental integrase inhibitor
- Dose ranging human safety P1
- NHP model efficacy studies complete

MPTs in the Pipeline

- Small Organic Molecules
- Broad Spectrum Natural Products
- Proteins/Peptides
- Non-Hormonal Contraceptives

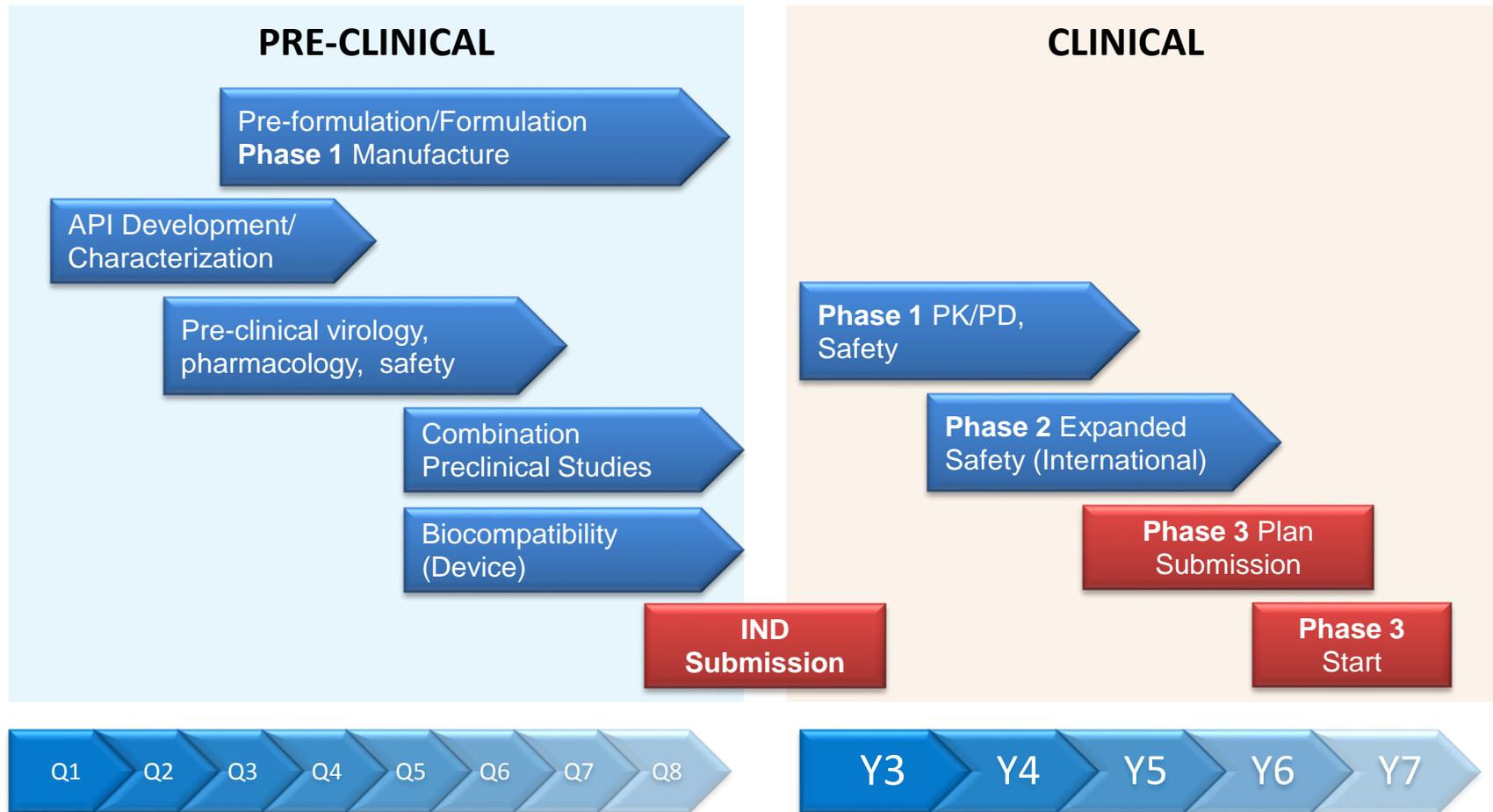


Single & Multipurpose Vaccines

- **Today:** *Single* purpose vaccines (HPV & HBV)
- **20 years:** Multivalent vaccines (HSV, HIV, Gonorrhea, Chlamydia, Trichomonas, other STIs), syphilis
- Contraceptive vaccines are not likely



MPT Product Development Timeline



Acknowledgments

INDIVIDUALS

- Bethany Young–Holt** (CAMI)
- Wayne Shields** (ARHP)
- Judy Manning** (USAID)
- Joseph Romano** (RWJ Group)
- Heather Boonstra** (Gutmacher Institute)
- Martha Brady** (Population Council)
- Nomita Chadhiok** (ICMR)
- Jessica Cohen** (PATH)
- Polly Harrison** (CAMI/AVAC)
- Anke Hemmerling** (UCSF/CAMI)
- Annette Larkin** (CONRAD)
- Wayne Shields** (ARHP)
- Kathryn Stewart** (CAMI)
- Alan Stone** (CAMI/MEDSA)
- Kevin Whaley** (Mapp Biopharmaceutical)
- Allen Wu** (Nanjing University)
- Susie Cornell** (Wits RHI)

SUPPORTERS

- Bill & Melinda Gates Foundation**
- Boston Consulting Group**
- Mary Wohlford Foundation**
- Microbicide Trials Network**
- National Institutes of Health**
- Public Health Institute**
- US Agency for International Development**
- Wellcome Trust**

