From Ideal to Real: What’s in the MPT pipeline?

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“New Products, New Paradigms: Combination Products for Women”
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Our challenge: *how to address the primary sexual and reproductive health needs of all women?*

1. Healthy timing & spacing of intended pregnancies
2. Protection against HIV
3. Protection against other STIs

*While taking into account changing needs and risks due to age, relationship status, and economic status*
Complexities of MPT product development:

### INDICATION
- Pregnancy
- HIV
- HSV
- HPV
- Gonorrhea
- Syphilis
- Chlamydia
- BV
- Candida
- Trichomonas

### MECHANISM OF ACTION
- Barrier
- Non-HC
- Anti-Microbial
- Anti-viral
- Probiotic
- Antifungal

### DOSAGE & ADMINISTRATION
- Vaginal gel
- Vaginal film
- Vaginal tablet
- Vaginal ring
- Non-IVR device
- Oral pill
- Implant
- Injection

Adapted from J. Romano presentation, *Multipurpose Prevention Technologies for Reproductive Health 2011 Symposium, Washington, DC*
May 5, 2011 MPT “Think Tank” of 30 FP/RH researchers

- Think Tank Description of a TPP:
  - How a proposed candidate product addresses critical attributes
  - Outline a framework for development given those specifications

- 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

**TPP Working Group Process:**

- Create tables of product attributes and parameters
- Solicit expert review regarding ideal and minimally acceptable thresholds (domestic and international researchers and providers)
- Consolidate consensus views
Developing TPPs for MPTs, cont.

TPP Working Group Outcomes:
- **Priority Indications**: Pregnancy + HIV; followed closely by HIV+HSV
- **Dosage Forms**: Major determining factor is PRODUCT ADHERENCE. Highest development priority: **Vaginal Rings**

Conclusions:
- **Defining broadly applicable attributes and parameters for all drug-drug or drug-device MPT products is challenging!**
  - The interplay of different attributes is complex and unique per product concept and design
- **It is possible to create general development priorities and fundamental design targets for such MPT products**
  - Useful to funders in terms of investment prioritization
  - Useful to developers in terms of R&D focus

What Reasons do Women Cite for Non-Use of Contraceptives in Demographic & Health Surveys?

Women with unmet need for modern contraceptives, 2008
148 million women living in Sub-Saharan Africa, South Central Asia, Southeast Asia

Access-related and other concerns (30%)

Method-related concerns (70%)

Source: Darroch, et al 2011; Contraceptive Technologies: Responding to Women’s Needs; Guttmacher Institute
Priorities for 1st-generation MPTs:

✓ “On demand” products:
  - Used around the time of intercourse
  - Appropriate for women who have infrequent sex, or who would like more direct control over their own protection

✓ Sustained release devices:
  - User-initiated, but do not require daily action
  - Should increase adherence, and therefore overall effectiveness
“On demand” Products: Gels

- **Tenovir Gel** (CONRAD)
  - First-ever vaginal microbicide shown to be effective in preventing HIV (39%) and HSV-2 (51%) (CAPRISA 004 proof-of-concept trial)
  - Coitally-dependent method: women in the study used the gel at least 12 hrs before and after sex, but not more than twice in 24 hrs
  - Confirmation trial (FACTS 001) has begun enrolling 2,600 HIV-negative 18-30 yr old women at nine sites in South Africa (Sponsored by CONRAD; funded by USAID, BMGF, and South Africa’s Dept of S&T. Product supplied by CONRAD and Gilead)
  - Results are expected in early 2014

- **MZL Combination Topical Gel** (Pop Council)
  - Combines MIV-150 + Zinc Acetate + the progestin LNG in carrageenan gel
  - Prevents pregnancy, HIV, HSV-2 and HPV (based on in vivo studies)
  - Provides effective protection for up to 24 hours
  - Gel optimization and initial PK in vivo is underway
**“On demand” Products: Devices + Active Agents**

**SILCS + TFV Gel**

1. **SILCS Contraceptive Barrier** (PATH, CONRAD, NICHD)
   - “One size fits most” silicone diaphragm that does not need to be fitted by a clinician; intended for OTC provision
   - 6-mo typical use pregnancy rate comparable to standard fitted diaphragm when used with a contraceptive gel (10.4%)
   - 5-yr shelf life; re-use for up to 3 yrs

2. **Plus TFV Gel** (CONRAD)
   - Use the SILCS barrier as a delivery device for TFV gel, reformulated to enhance contraceptive activity
   - Would provide a *non-hormonal method* of protection from pregnancy, HIV and HSV-2
   - Designed for effective protection for up to 24 hrs
   - Gel reformulation work is underway
Sustained-Release Devices: Combination Intravaginal Rings (IVRs)

- **30-day MZL Combination IVR** (Population Council)
  - Combines MIV-150 + Zinc Acetate + LNG
  - Demonstrated successful release in single-API rings, so MZL IVR will likely release all three APIs
  - The MZL IVR could prevent pregnancy, HIV and HSV-2

- **60-day Dapivirine + HC IVR** (IPM)
  - Combines the ARV dapivirine (DPV) with a hormonal contraceptive (HC)
  - DPV+HC ring formulation and testing are underway
  - The DPV+HC IVR could prevent pregnancy and HIV

- **90-day Tenofovir + LNG IVR** (CONRAD)
  - Combines tenofovir (TFV) with the hormonal contraceptive, LNG
  - TFV+LNG ring formulation and testing are underway; clinical studies in 2013
  - The TFV+LNG IVR could prevent pregnancy, HIV and HSV-2
These first-generation MPTs could...

- Simultaneously prevent pregnancy, HIV, HSV-2, and HPV.
- Provide a diversity of delivery & dosing options that will be **KEY** to meeting the different needs of women, and thereby expanding acceptability and use:
  - **MZL gel**: ideal method for women who would like a product they could use “on demand”, and that lasts up to 24 hours
  - **SILCS+TFV gel**: ideal method for women who would like a non-hormonal contraceptive product that they control, especially for intermittent sex
  - **Combination IVRs** (MZL, DPV+HC, TFV+LNG): ideal method for women who would like a highly effective product that requires minimal user involvement, and that provides continuous protection for 1-3 months
Other Relevant Ongoing MPT Activities:

- **Facilitating Regulatory Approval of MPTs** *(Population Council)*
  - Review existing guidance on combination products from Regulatory Authorities (RAs) such as the FDA, EMA, and ICH
  - Develop clarifying questions for the FDA and other RAs on approval pathways for MPTs
  - Convene technical meetings to discuss possible streamlined pathways for approval
  - Work with WHO to connect with other RAs in sub-Saharan Africa and south Asia on developing approval processes for MPTs

- **MPT R&D Pipeline and Gap Analysis** *(CAMI)*
  - Donor-led Scientific Agenda Working Group (product agnostic)
  - Review of MPT potential within the existing R&D pipeline for contraception, HIV prevention, and other STI prevention
  - Identification of gaps in MPT product R&D
  - Result in consensus statement and recommendations for donor investment in MPT R&D (Fall 2012 meeting)
In Conclusion

Multipurpose Prevention Technologies that simultaneously...

- Prevent unintended pregnancy
- Protect against HIV
- Protect against other STIs

...would enable women to address their own sexual and reproductive health risks as they change over time

Our Ultimate Goal:

Develop MPTs that are appropriate for provision and use in low resource settings, and that also meet the needs of women in the U.S., Europe, and other high resource settings

Thank you!