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
  - HC
  - Non-HC
  - Anti-Microbial
  - Probiotic
  - Anti-viral
  - Anti-fungal

- **DOSAGE & ADMINISTRATION**
  - Topical Peri-coital
  - Oral Peri-coital
  - Topical Daily
  - Oral Daily
  - Topical Sustained
  - Systemic Sustained

- **DELIVERY MODE**
  - 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*
Developing “Target Product Profiles” (TPPs) for MPTs

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%)
- Health / side effects: 22%
- Infrequent sex: 21%
- Postpartum: 17%
- Partner opposed: 16%
- Woman opposed: 10%
- No access / high cost: 8%
- Unaware of methods: 4%
- Perceived sub-fecund: 4%

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

- **Tenofovir 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
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!