Multipurpose Prevention Technologies (MPTs)

- An MPT is:
  - A single product with at least two SRH prevention indications
    - Contraception
    - HIV prevention
    - STI prevention (i.e. HSV)
    - Other health benefits

Graphic from: CAMI/PATH, Saving Lives with Multipurpose Prevention Technologies, 2010
# MPT Development Considerations

<table>
<thead>
<tr>
<th>Indication</th>
<th>Mechanism of Action</th>
<th>Dosage</th>
<th>Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>Antiviral</td>
<td>Daily</td>
<td>Topical (Vaginal)</td>
</tr>
<tr>
<td>HIV</td>
<td>Antimicrobial</td>
<td>Peri-coital</td>
<td>Ring</td>
</tr>
<tr>
<td>HSV</td>
<td>Antifungal</td>
<td>Sustained release</td>
<td>Gel</td>
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<tr>
<td>HPV</td>
<td>Hormonal</td>
<td></td>
<td>Tablet</td>
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<tr>
<td>Syphilis,</td>
<td>Non-hormonal</td>
<td></td>
<td>Film/Mesh</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>Barrier device</td>
<td></td>
<td>Systemic</td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td>Probiotic</td>
<td></td>
<td>Oral pill</td>
</tr>
<tr>
<td>Candida</td>
<td></td>
<td></td>
<td>Implant</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td></td>
<td></td>
<td>Injection</td>
</tr>
</tbody>
</table>

Adapted from: J. Romano/NWJ Group, 2012. *High-impact MPT products: Necessary attributes, development prospects, and challenges.* Available at CAMI-health.org
MPTs in the Pipeline

• “On-demand” products
  o Gels
  o Barrier devices

• Sustained release products
  o Vaginal rings
  o Long-acting injectables

• Other options
  o Implants, films, nanofibers, vaccines, non-hormonal contraceptives
“On-demand” MPTs

• Tenofovir gel (HIV + HSV-2) - CONRAD
  o CAPRISA 004 trial established proof-of-concept for ARV-based microbicides
    ▪ 39% effective against HIV; 51% effective against HSV-2
    ▪ 12 hours before and after sex; coitally dependent use
  o Confirmatory trial ongoing (FACTS 001); results in 2015

• SILCS Diaphragm with tenofovir gel – PATH/CONRAD/NICHD
  o Non-hormonal, barrier method of contraception + HIV + HSV-2
  o Barrier device also used to deliver tenofovir gel
  o Aims to provide protection for 24 hours

Source: J. Manning, AIDS 2012. From Ideal to Real: What’s in the MPT Pipeline. Available at CAMI-health.org
MPT Rings in Development

• 90-day tenofovir-levonorgestrel (LNG) ring – CONRAD
  o HIV + HSV-2 + pregnancy
  o 90 day sheep study complete
  o Phase 1 planned Q3-2013

• 90-day “MZCL” ring – Population Council
  o Contains the ARV drug MIV-150 along with zinc acetate, carrageenan and LNG
  o HIV + HSV-2 + HPV + pregnancy
  o Prototype development and preclinical evaluation ongoing
  o Additional formulations planned: 30-day & on-demand nanofibers
IPM’s MPT Ring

• 60-day dapivirine-LNG ring
  o HIV + pregnancy
  o Silicone matrix ring identified as lead formulation for 60-day use
  o Leverages expertise from the clinical development of monthly dapivirine ring (2 Phase III trials ongoing)
  o Focus on low-cost formulations, accelerated dev. timeline
  o Will guide design of more complex, longer-acting rings

Courtesy of Karl Malcolm, QUB

Matrix ring
Dapivirine (TMC120)

• Highly potent ARV (NNRTI)
• Developed by Janssen
  o Originally tested as oral therapeutic in 11 studies
• Licensed to IPM in 2004
  o Development as topical microbicide for HIV prevention
• 15 Phase I/II safety studies (dapivirine ring or gel)
  o Good safety profile in all studies to date
  o Data on more than 700 study participants before efficacy studies
• Dapivirine Ring Licensure Program started in 2012
Why Levonorgestrel (LNG)?

• LNG selected as contraceptive hormone due to:
  o Profile of continuous use
  o Suitability for formulation in matrix rings
  o Extensive clinical experience with continuous use
  o Good vaginal preclinical data and some clinical data on vaginal use
Daily Dapivirine Release from Matrix Rings

- 100 mg DAP
- 150 mg DAP
- 200 mg DAP
- 25 mg DAP (Ring-004)
Daily Levonorgestrel Release

Low Dose Ring
- 16 mg LNG
- 200 mg DAP; 16 mg LNG

35 µg/day target

High Dose Ring
- 32 mg LNG
- 200 mg DAP; 32 mg LNG

70 µg/day target
MPT Ring Regulatory Strategy

• Regulatory MPT program goals
  o Full leverage of existing safety and efficacy data from dapivirine ring program
  o Combine with currently available data on levonorgestrel products

• FDA pre-IND meeting planned for late 2013
  o Validate plan to bridge HIV prevention efficacy on the basis of PK
  o Gain agreement on preclinical and clinical development plans through product approval
IPM’s MPT Ring: Next Steps

• Formulation and polymer selection supports evaluation of 60-day use
• Prototypes currently being evaluated in preclinical studies
• Phase I clinical study planned in Q3-2014
• Potential development of extended use ring (up to 12 months) using core-sheath design
MPTs: Addressing Women’s Health Needs in Tandem

- Protection against HIV, unintended pregnancy and/or STIs
- On-demand and long-acting options could help ensure women have products that fit their unique lifestyle
- Potential to be more cost-effective, convenient
- Combining indications in one product may make protection more appealing and/or acceptable to women
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Questions