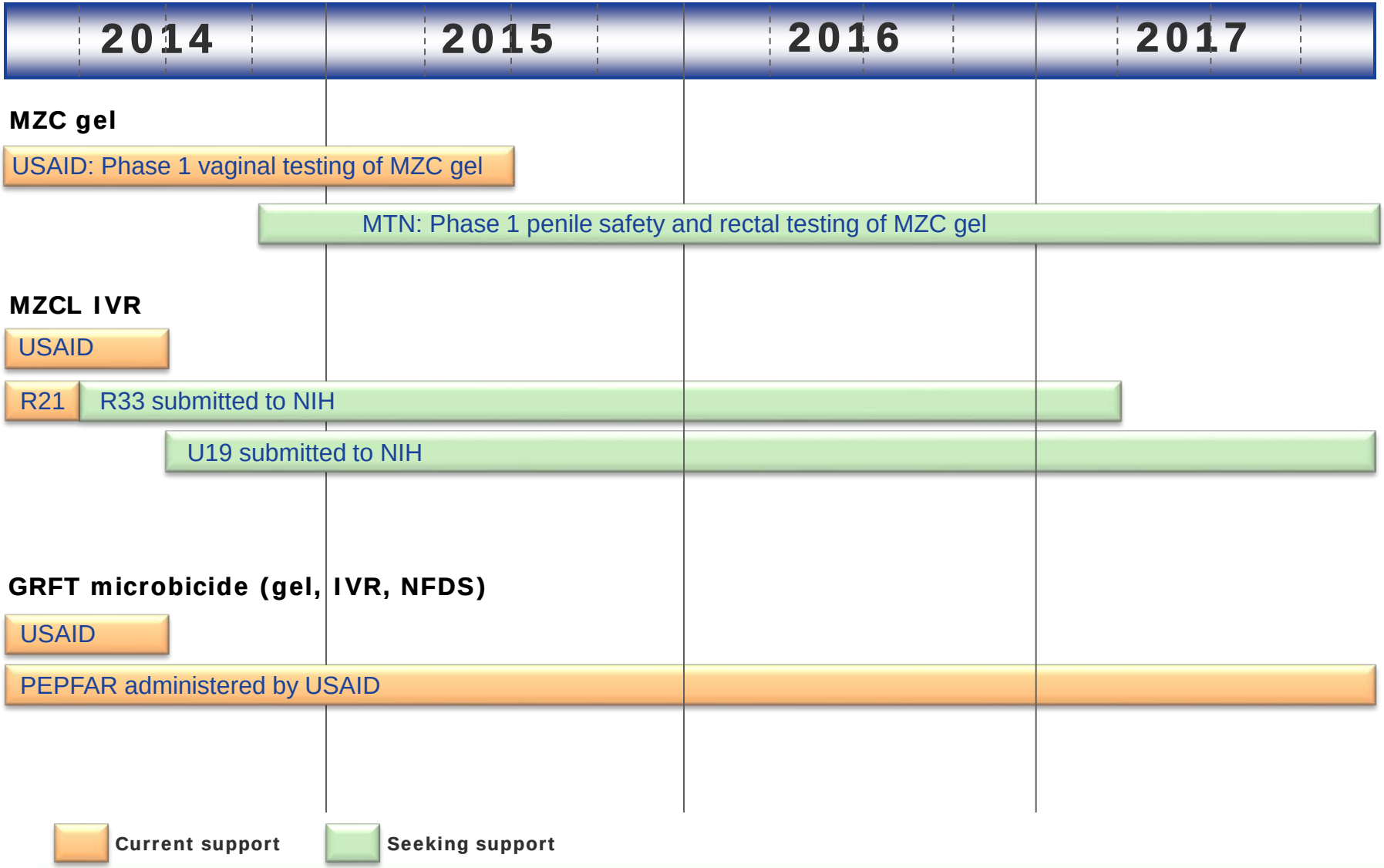
MZC Gel for the Prevention of HIV, HSV-2, and HPV

MTN Annual Meeting
February 24, 2014
Tom Zydowsky

Population Council

Council's Product Pipeline



Council's Microbicide Strategy

- Maximize public health impact of our products
  - Target HIV and STIs that increase risk of HIV acquisition and transmission (i.e., HPV and HSV-2)
  - Target STIs other than HIV that are major health risks
  - Provide sustained and on-demand delivery, contraceptive and non-contraceptive options
  - Minimize cost of final product
  - Reduce demands on user and health system, e.g., non-ARV based microbicide
- Develop one product for rectal and vaginal use

MZC Rectal and Vaginal Gel to Prevent HIV, HSV-2, and HPV

- On demand gel for rectal *and* vaginal use
  - 50µM (0.002%) **M**IV-150
  - 14mM (0.3%) zinc acetate (**Z**A)
  - 2.8% **C**arrageenan
  - Preservative: 0.2% methyl paraben
  - Neutral (pH ~6.8): 25mM sodium acetate buffer
  - Nearly iso-osmolar (250-550 mOsmol/kg)

MZC Gel Component Properties

- MIV-150 (**M**)
  - NNRTI with good resistance profile (*in vitro* and *in vivo*)
  - Prior human experience (4 oral trials)
- ZA (**Z**)
  - RTI with good resistance profile
  - *In vivo* activity against SHIV-RT and HSV-2
  - Significant human experience (FDA oral drug, GRAS)
- Carrageenan (**C**)
  - *In vivo* activity against HPV
  - Safe (GRAS) and acceptable in humans
- **MZC** Combination
  - Enhanced *in vivo* anti-SHIV-RT and -HSV-2 activity compared to individual components

MZC Gel: Pre-Clinical Efficacy

- Inhibits HIV, HSV-2, and HPV *in vitro*
- Blocks cell-free and -associated SHIV-RT infection of macaque vaginal explants (not affected by SP)
- Blocks cell-free HIV infection of human cervical explants
- Significantly reduces rectal and vaginal HSV-2 and HPV infection in mice
- Protects macaques against rectal and vaginal SHIV-RT infection and vaginal HSV-2 infection

MZC Gel: Non-GLP Rectal and Vaginal Safety Studies

- No damage to cells or ectocervical tissues *in vitro*
- No damage to mouse rectal or vaginal mucosa after a single application
- No increased HSV-2 susceptibility after once daily vaginal dosing for 7d
- Reduced the viability of epithelial cells at highest concentration tested
- 5-Day rectal and vaginal studies in macaques ongoing

GLP Safety Studies

- MIV-150: Completed for oral trials
- MZC gel: Completed for vaginal trials
  - 14-Day RVI
  - 28-Day toxicity studies in rabbits with TK
  - 28-Day toxicity studies in rats with TK
- MZC gel: Needed for rectal trials
  - Toxicity studies in rabbits and rats with TK

Council Capacity and Expertise

- In house gel manufacturing
  - GMP facility fully qualified November 2013
  - Industry experienced analytical and manufacturing teams
  - Capacity for Phase 1 gel; seamless tech transfer to established CMO partner for Phase 2+
- Project Management
  - Dedicated portfolio manager to track manufacturing activities and time lines
- Regulatory
  - RA and QA/QC to support and oversee manufacturing and interface with FDA

MZC Gel Summary

- Safe rectally and vaginally (iso-osmolar)
- Effective against a broad spectrum of STIs in animals, rectally and vaginally
- MZ combination exhibits increased anti-HIV activity and reduces drug resistance issues
- First in human rectal studies proposed
- Penile safety study will inform and accelerate development of MZC/MZCL IVRs

Thanks