MTN Protocol 002 Proposal:
Maternal Pharmacokinetics and Placental Perfusion of Tenofovir/PMPA Gel

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Microbicides developed to:
- Prevent HIV/STI transmission
- Intended for sexually-active women
- Planned widespread availability - OTC

Pregnancy common among:
- Young sexually-active women
- Cohort matches eventual users

Sexual activity common in pregnancy/early PP – multiple partners not unusual
- Solberg. NEJM 1973:288
- Klebanoff. Lancet 1984
- Read. AJOG 1993;168
- Rowland. Can Fam Phys 2005;51
Rationale - cont’d

- Pregnancy high-risk condition: HIV acquisition
  - Gray. Lancet 2005;366

- Pregnant women:
  - Rx and OTC medications used frequently
    - Andrade. AJOG 2004;191
    - Werler. AJOG 2005;193

- Practical:
  - If microbicides available
    - Pregnant women will use
    - (?)… Need for pregnancy test to use them

- Role for use in HIV(+) gravidas to decrease Maternal-Child perinatal HIV transmission
Goal/Specific Aims

- **MTN: Proactively assess formulations in pregnancy**

1. Assess term pregnancy maternal single-dose PK of Tenofovir/PMPA gel
   - ? Altered/increased absorption in late pregnancy
   - Compare to non-pregnant recent historic controls

2. Assess placental transport (fetal exposure) of single-dose Tenofovir/PMPA gel
Proposal

- Phase I, open label, Pharmacokinetic and safety evaluation
- 10 Healthy term HIV (-) (≥ 37 gestational weeks) parturients
  - Scheduled elective cesarean sections
  - No suggestion of placental disease
    - No IUGR, DM, HTN, CTD, etc.
- Single-site – MWH in PGH
Regimen:

- Single-dose Tenofovir (TFV) gel (40 mg)
- Placed vaginally in CS Pre-operative holding area
- Maternal PK
  - Baseline, 1 hour, 2 hour, 4 hour, 8 hour, 12 hour, and 24 hour
- Fetal TFV concentration assessment at time of CS
  - Amniotic Fluid
  - Cord Blood
Proposal cont’d

Endpoints:
- Detectable maternal plasma TFV
  - HPLC assay
- Detectable fetal cord blood &/or Amniotic Fluid TFV levels
  - HPLC assay

Other Analysis:
- Compare 3rd trimester single-dose absorption to non-pregnant absorption
  - Recent TFV gel PK (Mayer et al. AIDS 2006;20)
Future Directions

- Pending favorable PK/safety data in initial pregnant Phase I
  - Phase I, Placebo-controlled, multi-dose PK, tolerability, safety & placental perfusion study:
    - late 3rd trimester healthy gravidas scheduled for upcoming term CS