Regulatory Perspective on Issues in Pre-Exposure Prophylaxis Research

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Scenarios For HIV Prevention

- Approved Oral ARV for Treatment and Prevention (e.g. Truvada)
- Approved Oral ARV for treatment ⇒ Long Acting Injectable or other delivery system
- New Investigational Product

Perspectives on HIV Prevention Trials

- Clinical trials are needed for HIV prevention indications
  - Approved formulation, new formulation of approved drug, new investigational agent or “cousin” drugs
  - Exposure response for prevention not known and no validated biomarkers

- Standard prevention package for PrEP trials
  - What is the standard of care for PrEP globally?
  - Should oral PrEP be provided or offered as part of standard prevention package in trials?

Trial Design Considerations

Placebo vs Active control

Placebo control

- Superiority design (+/- background Truvada use)
  - Can placebo controlled trials still be done in:
    - Women given prior inconsistent trial results

Active control – Truvada vs New Drug

- Superiority or Non inferiority (NI) designs
  - Defining NI margin for trial in women is problematic given prior inconsistent trial results
  - Defining NI margin for MSM comparing Truvada to new product is possible and requires large sample size
- Looking for designs to reduce trial sample sizes to manageable levels
  - NI trials where new drug is not expected to be superior will be inordinately large under stringent statistical sample size calculations

Other Considerations

- Long acting injectable ARVs can be developed in the absence of an immediate release formulation
- Subject retention imperative to overall safety and efficacy evaluation
  - Pre-trial feasibility assessments (# of injections, frequency, volume of injections)
  - Engagement of community, subject and trial site support