What would you do?

CONTEXT: Tenofovir Gel

- CAPRISA 004
  - 39% fewer HIV infections in women using before and after sex compared to placebo
  - True effectiveness could be low as 6% or high as 60% (confidence interval)
- VOICE testing tenofovir gel used daily
  - Study taking place in SA, Uganda and Zimbabwe
  - Results expected early 2013, but DSMB could stop the study at any time for efficacy, safety or futility
- FACTS 001 testing same regimen as CAPRISA 004
  - just getting underway in SA
- FDA and MCC could approve tenofovir gel based on results of VOICE and FACTS 001
  - It would take about 2 years before the gel would be available

CONTEXT: Oral PrEP

Truvada

- Effective in MSM – 42-44% fewer HIV infections (iPrEx)
- Inconclusive in high-risk women – study stopped for futility (FEM-PrEP)
- Highly effective in serodiscordant couples – 73% fewer infections (Partners PrEP)
- Effective in heterosexual men and women – 62.6% fewer infections, but small study (TDF2)
- Don’t know yet in women – Truvada arm ongoing in VOICE

CONTEXT: Oral PrEP

Tenofovir

- Highly effective in serodiscordant couples – 62% fewer HIV infections (Partners PrEP)
- Not effective in women in VOICE – arm stopped because oral tenofovir no better than placebo
- Don’t know yet in IDUs – CDC Bangkok Study ongoing – results in 2012

Scenario #1

- Uganda is preparing to incorporate oral PrEP into its national HIV prevention program. Initially, the program will be targeted to serodiscordant couples.
- The ASPIRE research team in Uganda has submitted the study protocol to its IRB/EC for review. The IRB will approve the protocol if oral PrEP is included in the standard HIV prevention package.
- At the same time, advocates are pressuring researchers to provide oral PrEP at all ASPIRE sites–in Malawi, SA, Zambia and Zimbabwe.
- It's uncertain whether these countries will adopt oral PrEP into national programs. But in Malawi, the use of ARVs for prevention is strongly opposed.

As the lead investigator for ASPIRE, what would you do?

- **Should oral PrEP be offered to participants in Uganda only?**
- **Should oral PrEP be offered to women at all trial sites, including in trial-site countries where oral PrEP is not the national standard or practice?**

Scenario #2

- Uganda is preparing to incorporate oral PrEP into its national HIV prevention program. Initially, in serodiscordant couples.
  - The ASPIRE trial site in Uganda will provide oral PrEP to participants as part of the standard HIV prevention package.
- In Zimbabwe, government health officials have not yet decided whether to offer oral PrEP on a national level.
- When the local IRB/EC in Zimbabwe meets to discuss the ASPIRE protocol, its members are divided about the issue of oral PrEP.
  - Some feel it's unethical <u>not</u> to provide oral PrEP to ASPIRE participants, based on the results of Partners PrEP.
  - Others say there is not enough evidence to support its use; also, it would be unethical to provide an intervention that may not be available to women after the trial is over.

As the one IRB member who can break the tie, what would you do?

- **Side with those who believe oral PrEP should be offered to participants in Zimbabwe?**
- **Side with those who believe oral PrEP should <u>not</u> be offered?**

Scenario #3

- Tenofovir gel is found effective in VOICE. FACTS 001 stops early after a review of its data also finds tenofovir gel is effective.
- It's assumed tenofovir gel will be approved by the U.S. FDA and the SA MCC. If approved, it'll be 2 more years before widely available.
- ASPIRE has already enrolled more than 2,000 women and on target to have results before tenofovir gel could be available.
- The IRB/EC for one of the ASPIRE trial sites requests a change in design –instead of comparing the dapivirine ring to a placebo ring, the study should compare dapivirine ring to tenofovir gel.
- The researchers are concerned that this will make it difficult to get clear answers about whether the dapivirine ring is safe and effective.
  - The original design (with a placebo) provides the kind of data that regulatory authorities need to consider the ring's approval.

As the chair of this particular EC, what would you do?

- **Would you let ASPIRE continue, with half of the women using the dapivirine ring and the other half using a placebo ring ?**
- **Would you feel differently if tenofovir gel were already approved and knew it would be available soon?**