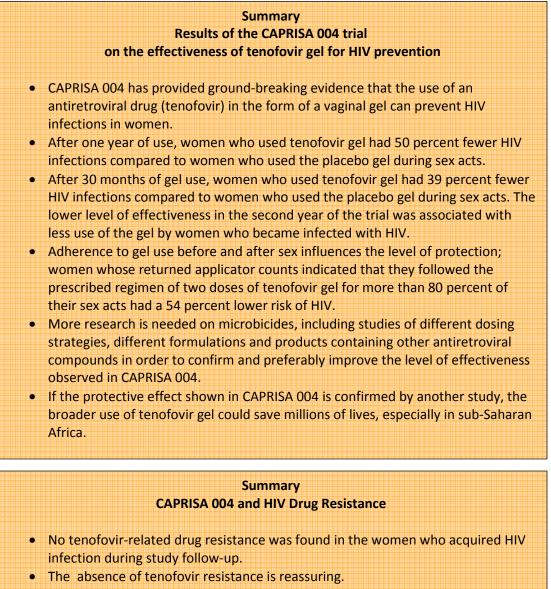
#### CONFIDENTIAL Embargoed until July 20: 1pm Central European Summer Time/13h00 South African Standard Time/ 7am U.S. Eastern Daylight Time

# CAPRISA 004 Trial Summary Sheet of Facts



- Drug resistance testing methods conventionally used to identify drug resistance in patients on antiretroviral therapy were used in CAPRISA 004.
- We are currently using new highly sensitive DNA technologies to test for rare drug resistant strains; these results are expected in a few months.

Suggested Citation: FHI and the Centre for the AIDS Programme of Research in South Africa. *CAPRISA 004 trial: Summary Sheet of Facts.* Research Triangle Park, NC USA, July 2010.

#### Summary

## CAPRISA 004 Trial and the Impact of Tenofovir Gel on Herpes Simplex Virus Type-2 Infections

- Tenofovir gel provided a 51 percent protective effect against the acquisition of the herpes simplex virus (HSV-2) among trial participants—an encouraging result for the prevention of genital herpes.
- If this protective effect is confirmed by another study, the broader use of tenofovir gel could reduce the prevalence of HSV-2, especially among the most vulnerable populations of the world.
- The prevention of HSV-2 also has consequences for HIV prevention because people who are infected with HSV-2 are more likely to acquire and transmit HIV.
- CAPRISA 004 participants who were HSV-2 negative were consistently less likely to acquire HIV.
- Tenofovir gel reduces HIV risk in women with HSV-2 infection and in women without HSV-2 infection. The effects of tenofovir gel on HIV and HSV-2 infections are separate and independent of each other.

#### Summary Safety in the CAPRISA 004 Trial

- One of the primary goals of CAPRISA 004 was to establish the safety of 1% tenofovir gel when used by women to prevent HIV infection.
- Safety was monitored at enrolment and throughout the trial by CAPRISA staff members, by a Protocol Safety Review Committee, and by an independent Data and Safety Monitoring Board.
- There were 39 serious adverse events in the study, but none of these events were related to use of the study product.
- No kidney disorders—the most important tenofovir-related safety concerns were observed in CAPRISA 004.
- Mild, self-limiting diarrhea was more common among women who used tenofovir gel (16.9 percent) compared to women who used the placebo gel (11.0 percent).
- No tenofovir resistance was observed among the women who became infected with HIV in the tenofovir group.
- No increase in hepatic flares was observed in participants infected with the hepatitis B virus (HBV).
- There were no safety concerns in the 54 pregnancies observed in the trial.
- Twelve cases of social harm were reported during the trial.
- There is no evidence that the participants decreased any HIV risk-reduction practices (such as condom use).

#### Summary CAPRISA 004 Trial and Pregnancy

- CAPRISA 004 was designed to (1) minimize pregnancies and (2) minimize exposure to tenofovir gel during a participant's pregnancy. Both objectives were achieved.
- CAPRISA 004 had a very low pregnancy rate compared to other microbicide trials.
- Women who became pregnant during the trial were immediately withdrawn from using the study product.
- Short-term exposure to tenofovir gel for up to one month in early pregnancy during the trial did not raise any safety concerns for the pregnant women or their babies.

### Summary CAPRISA 004 and Adherence to Study Product

- The CAPRISA 004 trial had good adherence—on average 72.2 percent of reported sex acts were covered by two doses of tenofovir gel.
- Although adherence is challenging to measure, accurate assessment of adherence is important because it influences the level of protection observed in a study.
- CAPRISA 004 measured adherence based on monthly self-reports and counts of used and unused gel applicators returned by the participants.
- Women who followed the prescribed regimen of two doses of tenofovir gel for more than 80 percent of their sex acts had a 54 percent lower risk of acquiring HIV.
- CAPRISA 004 used innovative methods to support adherence, including motivational interviewing techniques, to increase adherence to gel use.
- Future trials will need to place greater emphasis on enhancing and objectively measuring adherence in light of its substantial influence on the trial outcome.

For more information see <u>www.caprisa.org</u> and <u>www.fhi.org</u>.



