CONFIDENTIAL
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CAPRISA 004 Trial
Summary Sheet of Facts

Summary
Results of the CAPRISA 004 trial
on the effectiveness of tenofovir gel for HIV prevention

- CAPRISA 004 has provided ground-breaking evidence that the use of an antiretroviral drug (tenofovir) in the form of a vaginal gel can prevent HIV infections in women.
- After one year of use, women who used tenofovir gel had 50 percent fewer HIV infections compared to women who used the placebo gel during sex acts.
- After 30 months of gel use, women who used tenofovir gel had 39 percent fewer HIV infections compared to women who used the placebo gel during sex acts. The lower level of effectiveness in the second year of the trial was associated with less use of the gel by women who became infected with HIV.
- Adherence to gel use before and after sex influences the level of protection; women whose returned applicator counts indicated that they 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 HIV.
- More research is needed on microbicides, including studies of different dosing strategies, different formulations and products containing other antiretroviral compounds in order to confirm and preferably improve the level of effectiveness observed in CAPRISA 004.
- If the protective effect shown in CAPRISA 004 is confirmed by another study, the broader use of tenofovir gel could save millions of lives, especially in sub-Saharan Africa.

Summary
CAPRISA 004 and HIV Drug Resistance

- No tenofovir-related drug resistance was found in the women who acquired HIV infection during study follow-up.
- The absence of tenofovir resistance is reassuring.
- 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).

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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 www.caprisa.org and www.fhi.org.

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