FHI Statement on the FEM-PrEP HIV Prevention Study

FHI to Initiate Orderly Closure of FEM-PrEP

Monday, April 18, 2011

Following a scheduled interim review of the FEM-PrEP study data, the Independent Data Monitoring Committee (IDMC) advised that the FEM-PrEP study will be highly unlikely to be able to demonstrate the effectiveness of Truvada [emtricitabine (FTC) and tenofovir disoproxil fumarate (TDF)] in preventing HIV infection in the study population, even if it continued to its originally planned conclusion. FHI subsequently concurred and has therefore decided to initiate an orderly closure of the study over the next few months. The final analyses have not yet been conducted. At this time, it cannot be determined whether or not Truvada works to prevent HIV infection in women.

The FEM-PrEP clinical trial – implemented by FHI in partnership with research centers in Africa – is designed to study whether HIV-negative women who are at higher risk of being exposed to HIV can safely use a daily dose of a pill called Truvada to prevent infection. This study was funded by the United States Agency for International Development (USAID), with early funding from the Bill & Melinda Gates Foundation.

The FEM-PrEP outcome is surprising and disappointing, given a number of earlier studies suggesting the promise of pre-exposure prophylaxis (PrEP) using antiretrovirals. Most recently, the iPrEX study showed that use of Truvada can prevent infection in men who have sex with men at risk of HIV.

There are a number of possible reasons for the study findings, including low adherence to study regimen, a true lack of effect of the product among women (versus men who have sex with men), or other factors still to be determined. FHI will be conducting further analyses and will share additional findings in the coming months. The IDMC commended the trial team on a study conducted to a high standard with good follow-up and careful attention to good clinical practice and ethical standards.

Only preliminary FEM-PrEP data are available at this time:

- As of February 18, 2011 the study had screened 3,752 women and enrolled 1,951: 739 in Bondo, Kenya; 764 in Pretoria, South Africa; 432 in Bloemfontein, South Africa; and 16 in Arusha, Tanzania. The most common reason for women not being enrolled was

existing HIV infection. The overall HIV prevalence was 21 percent among women screened for enrollment across the sites.

- Preliminary data indicate about 90 percent of the participants were retained in the study.
- Adherence to study product was approximately 95 percent when the study product was available for use.
- Women reported an average of 3.7 vaginal sex acts in the 7 days prior to enrollment, consistent with the average of 3.6 acts reported during follow-up.
- As of February 18, the approximate rate of new HIV infections among trial participants was 5 percent per year. A total of 56 new HIV infections had occurred, with an equal number of infections in those participants assigned to Truvada and those assigned to a placebo pill.
- Women participating in FEM-PrEP used an effective method of contraception at the time of enrollment – 66 percent were using injectables and 30 percent were using oral contraceptives. The overall pregnancy rate was 9 percent; the highest pregnancy rates were among women using oral contraceptives.
- The use of Truvada in FEM-PrEP was associated with some known side effects that were not serious.

Among study participants randomly assigned to the Truvada arm, observed pregnancy rates were higher than among women randomly assigned to the placebo arm. This is unexpected and inconsistent with known drug interactions involving tenofovir (TDF) and contraceptive hormones, and with known metabolic effects of emtricitabine (FTC). Possible explanations include differential pill adherence by group, previously undefined drug-drug interactions, chance, or a combination of factors (including yet unknown factors). FHI will conduct further analyses of these data.

FHI and its partners are especially grateful to the women whose willingness to participate and commitment to the study were essential. To the extent possible, all participants have been notified of the decision and are being asked to come to the study clinics for final visits. Study participants who became infected with HIV during the study are being followed by the study team for an additional year and are referred for appropriate medical care and treatment in their community.

When the follow-up of the HIV-uninfected women is complete in a few months' time, FHI will be conducting in-depth analyses of study data and blood specimens collected during the study to examine the factors contributing to the observed outcomes. FHI will also collaborate with scientists conducting other PrEP studies to compare findings and to better understand the results.

When available, the final results from FEM-PrEP will make a strong contribution to our understanding of the use of antiretrovirals for HIV prevention. FHI, USAID and research partners in Africa are committed to finding new technologies and developing new strategies to protect women from HIV.

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For more information, see www.fhi.org.

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About FEM-PrEP
FEM-PrEP is a randomized, placebo-controlled, clinical trial of the effectiveness of daily, oral Truvada for HIV prevention among HIV-uninfected women in Kenya, South Africa and Tanzania. Truvada combines two antiretroviral drugs--emtricitabine (FTC) and tenofovir disoproxil fumarate (TDF)--in a single pill that is taken once a day. Truvada has been proven safe and effective as a treatment for HIV-positive people. FEM-PrEP has a strong socio-behavioral and community engagement component. The study is funded by the U.S. Agency for International Development (USAID), and received early support from the Bill & Melinda Gates Foundation.

About FHI
FHI is a global health and development organization whose science-based programs bring lasting change to the world's most vulnerable people. Since 1971, FHI has worked with 1,400 partners in 125 countries, forging strong relationships with governments, diverse organizations, the private sector and communities. By applying science to healthcare programs and clinical research, FHI is helping countries make measurable progress against disease, poverty, and inequity—improving lives for millions.