Pre-Exposure Prophylaxis (PrEP) for HIV Prevention ▪ A Fact Sheet for Advocates ▪ December 2008

AVAC
AIDS Vaccine Advocacy Coalition

What is PrEP?

Pre-exposure prophylaxis (PrEP) refers to an experimental HIV prevention strategy that would use anti-retrovirals (ARVs) to protect HIV-negative people from HIV infection. In this experimental strategy, people would take ARVs before they were exposed to HIV, with the goal of lowering their risk of infection.

Studies of PrEP strategies in non-human primates have shown a reduced risk of infection among animals that receive ARVs prior to exposure to a simian form of HIV. These studies took small groups of animals pre-treated with ARVs—pre-exposure prophylaxis—and compared them with animals that did not receive any ARVs and were exposed to the same virus. In these studies, there was evidence of protection from PrEP. Another rationale for PrEP comes from strategies to prevent mother-to-child transmission, which use ARVs given to the mother and the infant to help reduce the risk of transmission.

Which drugs are being tested for PrEP?

There are two ARVs being tested in PrEP trials; tenofovir disoproxil fumarate (TDF), commercially known as Viread® and TDF + emtricitabine (FTC), commercially known as Truvada®. Both drugs are ARVs that have been approved for use in treating HIV infection—they are safe for use in HIV-positive people but information on the safety of daily use of these ARVs among HIV-negative individuals is still needed.

Scientists have focused on these drugs because they have proven safe for use in humans for HIV treatment, remain in the blood stream for long periods of time, require once-daily dosing, and have unique resistance profiles—meaning that if someone developed drug resistance to TDF or TDF+FTC, he or she would still be able to use many other types of ARVs.

How is PrEP tested to see if it reduces risk of HIV?

All HIV prevention trials use similar trial designs—trials are conducted in communities where the rate of new HIV infections—the incidence—is well documented prior to the study launch; trial volunteers are randomly assigned to either the experimental arm, which receives the strategy being studied, or to the control arm; both arms receive the same package of prevention counseling and services, which includes provision of condoms, treatment of sexually-transmitted infections, and behavior change counseling. Clean needles and harm-reduction services should be provided in injection-drug user studies in order to meet basic ethical requirements. Participants are never encouraged to have unsafe sex or to expose themselves to HIV.

After enrollment, all volunteers are followed over time, with periodic study visits where HIV tests and other lab analyses may be conducted. The data are periodically reviewed by a Data and Safety Monitoring Board, an independent body. At the end of the study, researchers look at the numbers of new HIV infections in the experimental and control arms to see if there is a difference. If the strategy is effective, the number of new infections should be significantly lower in the experimental arm.

For additional information and up-to-date resources on PrEP research around the world, please visit www.prepwatch.org.

In the case of PrEP trials, neither the study volunteers nor the study staff knows who is receiving the active drug and who is receiving the placebo – in this case, pills that look identical to the ARVs but have no effect. Volunteers are closely monitored for side effects associated with the medications.

In order to get a clear picture of whether PrEP is a viable prevention strategy, data on safety and efficacy are needed on different populations: men who have sex with men, injection-drug users, and heterosexual men and women.

What is the state of PrEP research today?

As of December 2008, there are five human clinical trials of PrEP ongoing and two to begin in 2009:

Location	Sponsor/ Funder	Population (mode of exposure)	Intervention arms	PrEP strategy(ies) being tested	Status / Expected completion
United States	CDC	400 gay men and other men who have sex with men (penile/rectal)	1	TDF	Fully enrolled – Ongoing / 2009
Thailand	CDC	2,400 injecting drug users (parenteral)	1	Tenofovir disoproxil fumarate (TDF)	Enrolling / 2010
Brazil, Ecuador, Peru, South Africa, Thailand, US (iPrEX Study)	NIH, BMGF	3,000 gay men and other men who have sex with men (penile/rectal)	1	TDF+FTC	Enrolling / 2010
Botswana	CDC	1,200 heterosexual men and women (penile and vaginal)	1	TDF+emtricitabine (FTC) (switched from TDF Q1 2007)	Enrolling / 2011
Kenya, Uganda (Partners PrEP Study)	BMGF	3,900 serodiscordant heterosexual couples (penile and vaginal)	2	TDF; TDF + FTC	Enrolling / 2012
Kenya, Malawi, South Africa, Tanzania, additional sites TBD (FEMPrEP)	FHI, USAID	3,900 high-risk women (vaginal)	1	TDF+FTC	Planning / 2012 Anticipated start Q1/2009
Southern Africa, sites to be determined (VOICE Study)	MTN, NIH	4,200 sexually active women (vaginal)	3	TDF; TDF+FTC; TDF gel	Planning / 2012 Anticipated start Q1/2009
BMGF – Bill & Melinda Gates Foundation; CDC - US Centers for Disease Control; FHI – Family Health International; MTN – Microbicide Trials Network; NIH – US National Institutes of Health; USAID – United States Agency for International Development					

Challenges and Next Steps

- PrEP is still an unproven strategy that must be tested in clinical trials to see if it is effective.
- The current studies will not provide definitive answers about PrEP safety and efficacy in all populations. A clear research agenda of PrEP trials is needed to ensure all of the critical questions are answered in a timely manner.
- While the drugs currently being tested in PrEP trials have favorable resistance profiles, researchers must continue to monitor for resistance among PrEP trial participants who may seroconvert and require other ARVs for treatment.
- Work needs to be done in communities where research is planned or is being conducted in order to increase their understanding of clinical research, including how prevention trials are designed. Also, more efforts are needed to ensure that these studies are scientifically sound, meet the highest ethical standards, and are conducted with full community participation.

For an in-depth discussion on the topic of PrEP, please see AVAC's report, *Anticipating the Results of PrEP Trials* (August 2008), at www.prepwatch.org or email avac@avac.org.

AVAC is a non-profit, community- and consumer-based organization that uses public education, policy analysis, advocacy and community mobilization to accelerate the ethical development and global delivery of AIDS vaccines and other HIV prevention options.