Division of Dockets Management (HFA-305) Food and Drug Administration 5630 Fishers Lane, rm. 1061 Rockville, MD 20852

RE: Docket Number, FDA-2012-N-0218 - Efficacy Supplement for New Drug Application (NDA) 21-572, TRUVADA (emtricitabine/tenofovir disoproxil Fumarate or "TDF/FTC") Tablet - Indication for Pre-Exposure Prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection. Antiviral Drugs Advisory Committee (Committee) Meeting May 10, 2012.

To the Antiviral Drugs Advisory Committee and FDA:

Thank you for this opportunity to provide information to the Committee and to FDA regarding the efficacy supplement for pre-exposure prophylaxis (PrEP) for TDF/FTC (Truvada). We represent HIV/AIDS and health organizations across the United States and request that you recommend approval of the indication for adult men and women in accordance with the post marketing plans described in these comments.

PrEP will allow a medically supervised option to be used in conjunction with other behavioral and non-pharmaceutical prevention options to protect against a serious life threatening illness. PrEP can be significantly beneficial for HIV-uninfected men and women who are unable to consistently use standard prevention strategies, particularly male and female condoms; reasons for which vary considerably, but often due to the fact that their partners control the timing of sex and uses of such devices.

In this country, over 50,000 annual HIV infections occur despite our best efforts to prevent them. The President's National HIV/AIDS Strategy (NHAS) states:

We must also move away from thinking that one approach to HIV prevention will work, whether it is condoms, pills, or information. Instead, we need to develop, evaluate, and implement effective prevention strategies and combinations of approaches¹

Adding a new biomedical option assists in that government endorsed program by expanding choices and combinations typical of other health prevention efforts. Our detailed remarks on approval and post marketing conditions follow.

¹ http://www.whitehouse.gov/sites/default/files/uploads/NHAS.pdf

1. Indication

We support approval of the efficacy supplement for TDF/FTC (PrEP) with appropriate labeling cautions and supportive post-marketing requirements to prevent HIV-1 infection in all adult men and women. Data from the multiple clinical trials that this Committee has before it for review are consistent: HIV uninfected men and women who are at risk of HIV-1 exposure through sexual contact and who take daily TDF/FTC—as prescribed, along with counseling and standard prevention tools—reduce their likelihood of infection substantially and to a much greater degree than if they had relied on counseling and standard protection alone.

Published and scientific reported data from three trials demonstrate this efficacious effect in multiple settings and populations. When participants in these and other studies did not adhere to daily oral PrEP consistently – as recently demonstrated in another trial of PrEP where adherence was confirmed to be negligible – benefits do not accrue. As recently reported intracellular drug level data indicate, good adherence can result in efficacy rates of up to 90 percent or more. Adherence, however, is an operational concern that can be addressed within the healthcare setting.

2. Safety

PrEP has been shown to be safe in all clinical trials including reported trials where lack of adherence correlated with the absence of efficacy. Safety concerns attached to PrEP include theoretical emergence of drug resistance if undetected infection occurs during use of drug, adverse effects, and toxicities suggested by certain markers. In practice, should the new indication for TDF/FTC be approved these concerns may be addressed through cautions within the label and by Risk Evaluation and Mitigation Strategies (REMS) and other supportive post-marketing requirements.

Consistent with the marketing requirements applicable to other products mitigating risks in similar contexts, we request that approval require:

- A variety of plain language medication guides and educational initiatives suitable for different populations;
- Post marketing surveillance including data collection on adherence as well as safety tracking and reporting;
- Discussions with FDA, public representatives, clinical investigators and the manufacturer to determine the need for further manufacturer post marketing study; and
- Labeling conditions regarding appropriate intervals for monitoring of biological markers and HIV-1 infection.

3. Education, Prescriber Information, Supportive Requirements.

In most FDA approval situations the drug manufacturer produces informational and educational requirements for prescribers and patients. Given that behavioral, cultural and situational contexts around sexual risks may vary tremendously among PrEP users, we request that the Committee and FDA include community input representative of the men and women who have and are most likely to be prescribed PrEP in processes designed to negotiate the content and breadth of educational materials and not engage in such negotiations solely between the manufacturer and FDA.

We appreciate your consideration of these comments. Mitchell Warren serves as the contact person for this letter and can be reached at mitchell@avac.org or 1-646-369-1467

Sincerely,

AIDS Foundation of Chicago AIDS Project Los Angeles AIDS United AVAC: Global Advocacy for HIV Prevention Bay Area Perinatal AIDS Center Black AIDS Institute The Fenway Institute International Rectal Microbicide Advocates **Justice Resource Institute** National Black Gay Men's Advocacy Coalition (NBGMAC) National Minority AIDS Council (NMAC) Project Inform San Francisco AIDS Foundation SHERO Empowerment Network SisterLove **Treatment Action Group**