

## **New Hope for Women to take Charge of HIV!**

CAPRISA (Centre for the AIDS Programme of Research in South Africa) recently released results of a **clinical trial**, where they studied whether a vaginal gel containing **1% tenofovir** could prevent women becoming infected by HIV. Their results have generated great excitement as they showed that using the **microbicide** gel led to a significant reduction in HIV infection. Levels of HIV infection were reduced overall by 39% in the three year period of the study. In the group of women that kept to the specified routine the best (80% adherence), the level of HIV infection was reduced by 54%.

While a 54% reduction in HIV infection through regular use of the gel may seem like the chance of preventing infection is as good as tossing a coin, these results are significant. This study makes a significant stride in potentially providing a much needed tool to women to protect themselves against infection when their relationship does not. Further studies of different concentrations and different combinations of active ingredients and frequency of application may improve levels of protection. While condoms offer a proven high level of protection, they are dependent on the male partner's willingness to use them. These results mean that women who cannot persuade their partners to use condoms or to be faithful to them may have some means of protecting themselves against becoming infected by HIV. In the next 20 years, tenofovir gel could prevent 1.3 million new HIV infections and over 800,000 deaths in South Africa alone.

The CAPRISA 004 trial is the first microbicide trial that was co-funded by two governments, the South African and United States government. TIA (The Technology Innovation Agency), formerly LifeLAB, has provided funding to the amount of R8.5 million since the project started. Funding was also received from USAID (the United States Agency for International Development). The product was supplied by CONRAD, an international organisation that aims to improve the reproductive health especially in developing countries ([www.conrad.org](http://www.conrad.org)). Collaborating support was received from the global health and development organisation, FHI ([www.fhi.org](http://www.fhi.org)). TIA continues to support the study and holds a royalty free licence for the manufacture and distribution of the product, once it has passed all regulatory tests.

## Understanding some terminology:

### What is a microbicide?

Microbicides are applied to the vagina (or rectum) and prevent sexually transmitted infections (STI's). Previous clinical trials using microbicides have not shown any significant reduction in transmission of HIV. These include the Carraguard trial, which was the first anti-HIV microbicide to make it to phase III clinical trials but which failed to prevent transmission of HIV. The gel, containing an active ingredient derived from seaweed containing carrageenan, was tested in 6202 women in South Africa. There was no significant difference in infection between the women who received Carraguard and those who didn't.

Other phase II trials have been or are currently being conducted using tenofovir in a vaginal gel, but not for over an extended period of 3 years. Previously, a six month trial (HPTN059) was done in India and the US to determine if tenofovir was safe to use daily. The VOICE Study (Vaginal and Oral Interventions to Control the Epidemic) is another trial currently underway which will help determine whether using a vaginal gel containing tenofovir daily or taking an oral anti retroviral daily can reduce a woman's risk of becoming infected with HIV.

### What is tenofovir and how does it work?

Tenofovir is an antiretroviral (ARV). It is in the class of adenosine nucleotide analogs. In other words, it looks like the true nucleotide (adenosine) but is really a faulty imitation. When the virus enters the cell, it makes viral DNA which it fits into the host cell genetic material, allowing the virus to live permanently in the cell and make new viruses. Nucleotide analogs are incorporated into the growing strand of viral DNA by the enzyme reverse transcriptase because they look so much like the real nucleotide. However, because they are imitations, they stop further synthesis of the DNA. If the virus cannot make new genetic material, it cannot produce new infective viruses.

Tenofovir was approved in the US by the FDA (the Food and Drug Administration) for oral use in October 2001 for the treatment of HIV. It is formulated as tenofovir disoproxil fumarate (Viread<sup>®</sup>) as an oral treatment.

## What type of clinical trial was this?

The CAPRISA 004 trial was a **Phase II B** trial and a two-group, double-blind, randomized, placebo-controlled trial. This means the trial consisted of **two groups**; one using the 1% tenofovir gel and one using a placebo gel (a gel that contained no tenofovir or any other active ingredient). The women were assigned **randomly**, with none of the women knowing which group they were placed in and which gel they were using. **Double-blind** means that neither the participants nor the researchers knew which women were in which group. This eliminates bias by researchers in dealing with the patients.

Phase II trials are designed to study whether the drug works well and to continue looking at the safety of the drug that was studied in Phase I. They normally include a group of about 300 people, depending on the numbers needed to show statistically significant results. Phase II B is specifically designed to look at how well the drug works at the specific dosage. If Phase II trials are successful and indicate that the drug works and is safe, further trials are done in Phase III on larger groups (300-3000) and at many locations to determine more definitively how well the drug works.

A larger **phase III trial** must be done with this 1% tenofovir gel to confirm its safety and efficacy. Thereafter, regulatory approval from the Medicines Control Council (MCC) will be needed before it will be available as a product for widespread use.

Further information about the trial can be found on [www.caprisa.org](http://www.caprisa.org).