



## MICROBICIDE RESEARCH ALREADY BENEFITING THOUSANDS – EXPERTS



Dr Zeda Rosenberg, CEO of the International Partnership for Microbicides (IPM).

Microbicide research has 'reoriented' its approaches after two harmful and three futile trials almost 3 years ago and is currently hugely innovative, empowering entire communities through voluntary testing, education and new health infrastructure.

Dr Zeda Rosenberg, CEO of the International Partnership for Microbicides (IPM), was speaking at a media briefing by some of the world's leading microbicide researchers attending the International AIDS Society Conference in Cape Town this July.

'We clearly won't be able to treat our way out of the epidemic, so we have to develop effective preventative strategies,' she stressed in her introduction.

Initial microbicide trials, of Ushercell cellulose sulphate-based vaginal gel and Nonocynol 9 gel, were found to cause

lesions in the vagina, thus actually increasing the chances of HIV infection. Both were immediately stopped, but not without an AIDS denialist-driven public furore in the then hotly politically contested South African HIV prevention field.

Research by the London School of Hygiene and Tropical Medicine has shown that if just 20% of women at HIV risk used clinically effective microbicides just half of the time, it will prevent the infection of 2.5 million people over 3 years.

Current HIV prevention options fall way short of protecting vulnerable women who lack the power to insist their male partners use condoms or remain faithful. Abstinence is impractical for women who are married, who want to have children, or who are at risk of sexual violence.

So far only one early-generation microbicide, PRO 2000, which works via a non-specific entry inhibitor, electrostatically associating with the HIV virus and blocking it from attaching to target cells in the vagina, has proven 30% effective.

While not statistically significant (3% below the threshold), it has nevertheless provided major impetus for the concept of a topical microbicide preventing HIV infection in women during sex.

A much larger PRO 2000 Phase III clinical trial, led by a 'hopeful' Dr Sheena McCormack, a clinical epidemiologist

***No increase in domestic violence was reported around the use of gels, in dramatic contrast to the use of condoms.***



A recruiter for the Reproductive Health and HIV Research Unit in Edendale, South Africa, talks to community members about participating in an IPM trial.

Photo: Geoff Oliver Bugbee

from the UK Medical Research Council, currently covers 9 404 women from 6 locations in southern Africa. It is due to report results this November.

### 'Kick-starting' HIV services

McCormack told the luncheon briefing that her 600 staffers had screened more than 20 000 women for HIV, thus 'kick-starting' HIV services at each of the locations.

She said her Microbicide Development Programme (MDP) was unique because it integrated social and behavioural sciences, thus keeping tabs on what research partners and communities felt, and addressing issues such as transport and adherence.

So far women were reporting greater intimacy in their relationships (even though condom use was strongly encouraged). The PRO 2000 gel is biologically far less potent than ARV-based gels and does not require ongoing HIV testing.

Professor Helen Rees, Executive Director of the Reproductive Health and HIV Research Unit at the University of the Witwatersrand, leads a microbicide safety study in KwaZulu-Natal and is about to start at a VOICE (Vaginal and Oral Interventions to Control the Epidemic) study in Johannesburg. She said her team had established a network of trial sites, mostly doing microbicides, but, as importantly, able to do other pre-exposure prophylactic or vaccine work. 'These are invaluable research assets which are empowering young African researchers,' she emphasised.

The VOICE study looks at whether some of the same ARV medications used successfully for treating HIV are safe and effective for HIV prevention, as either a vaginal microbicide or an oral tablet. It also aims to find out which of these routines women are more likely to follow – a tablet by mouth once a day or applying a vaginal microbicide gel daily.

The study, which uses tenofovir (Viread) and tenofovir and emtricitabine (Truvada), was launched in August this year, enrolling 5 000 sexually active HIV-negative women at a host of southern African sites.

It is the first effectiveness trial of a microbicide used daily instead of only at the time of sex. One of its key aims is to find out if, and to what extent, HIV drug resistance is a possible risk for women who acquire HIV while participating in the trial.

The speakers emphasised that the ARVs used in the gels were chosen for their high genetic barrier for resistance and their long half-life. Rees said community 'buy-in' had been huge with long queues of often repeat applicants and very positive feedback from participants who reported reduced anxiety, ease of use, and increased sexual pleasure.

### Less domestic violence around gels than condoms

Dr Sharon Hillier, Director of Reproductive Infectious Disease Research at the University of Pittsburgh School of Medicine, said no increase in domestic violence was reported around the use of gels, in dramatic contrast to the use of condoms.

She said she had scoured ongoing studies for adverse events to reach this conclusion.

Rees stressed how vital it was to have political support 'at the highest level' in order to avoid conflict and suspicion over microbicide research among communities.

This was a possible allusion to the days of Health Minister Manto Tshabalala-Msimang, who used the stumbles and harm that occurred in early microbicide trials to bolster anti-Western drug arguments and champion the 'cause' of poor local women.

***The study found that HIV prevalence among local women aged under 20 leapt from 15% to 27% between 2001 and 2004, and among women between 20 and 29 rose from 39% to 66% (over the same period).***

One striking example of the dire need for a successful microbicide gel comes from a 2007 tenofovir study by the Centre for the AIDS Programme of Research in South Africa (CAPRISA) in the impoverished Mafakhatini district of Bulwer, KwaZulu-Natal.

The study found that HIV prevalence among local women aged under 20 leapt from 15% to 27% between 2001 and 2004, and among women between 20 and 29 rose from 39% to 66% (over the same period).

Rees said the ethics around HIV prevention research were heavily contested and 'we need to define what our obligations are for treatment and referral'.



*Dr Sharon Hillier, Principal Investigator, Microbicides Trials Network (MTN).*

*'It's not just about efficacy but social and behavioural, and we'll also have to consider how we make these products available long term,' she added.*

She said it was becoming increasingly important to take comprehensive measures and include all pre-exposure prevention tools, including taking into account the latest data around the protection offered by circumcision. 'We'll have to continually visit what we provide (to trial participants) – it's vital ethically. It's not just about efficacy but social and behavioural, and we'll also have to consider how we make these products available long term,' she added.

Rosenberg said the IPM had negotiated royalty-free contracts with drug companies in terms of cost, manufacturing and supply and were aiming for a high-volume, low-profit formula. She said the main costs came from manufacturing the actual gel, its applicators and shipping. 'But we're always looking at the materials used to try and drive costs down even further,' she said, adding that communities involved in the research would be the first to benefit should researchers make the hoped-for breakthrough.

**Chris Bateman**