



Global Campaign News – Issue #99

Welcome to the *Global Campaign News*! The *Global Campaign News* is a forum for international exchange on microbicide activities and information with an aim to build a more informed and integrated movement for microbicide development and other prevention options against HIV and other sexually transmitted infections. This and previous issues of *GC News* are available online at <http://www.global-campaign.org/gcarchives.htm>

In this issue:

Research update

Rectal microbicide protects monkeys from HIV-like virus
Following up on CONRAD's discontinued phase III trial of cellulose sulfate
Interpreting the recent PNAS article on Modeling ARV-based microbicides
MDP completes phase III trial enrollment

Highlighted Resources

Black AIDS Institute report: Left Behind. Black America: A Neglected Priority in the Global AIDS Epidemic
The HIV Vaccines and Microbicides Resource Tracking Working Group report: Sustaining the HIV Prevention Research Agenda

Advocacy in action

Spain announces 1.5 million Euros for microbicides research

Conference Highlights

Microbicides at Mexico
No youth, no change - Young people in Mexico lead the way forward on HIV responses

Research update



Rectal microbicide protects monkeys from HIV-like virus

Global

A novel ARV-based rectal microbicide, similar to the tenofovir-containing vaginal gel currently in clinical trials in South Africa, protects monkeys from simian immunodeficiency virus (SIV), an HIV-like virus that causes a disease similar to AIDS in primates.

In the August issue of *PLoS Medicine*, Martin Cranage of St. George's University of London and his colleagues exposed a type of monkey known as a rhesus macaque to SIV rectally. Some of the monkeys were pre-treated with rectal tenofovir gel two hours prior to SIV exposure, while other monkeys were treated with a placebo gel or received no treatment at all. Most of the monkeys treated with tenofovir gel (X of X) were protected against SIV, whereas a (Y of X) of the monkeys treated with placebo gel were

infected. All of the untreated monkeys acquired SIV. Rectal tissue taken from tenofovir gel-treated monkeys also showed considerable resistance to SIV infection in the laboratory. Although the ability of tenofovir gel to prevent transmission of HIV through vaginal or anal sex has yet to be proven in human trials, these data are some of the first to demonstrate the successful use of an ARV-based topical gel to prevent transmission of an HIV-like virus via the rectum.

The Global Campaign for Microbicides will continue to monitor the results of this and similar, and will update you regularly as new information arises. For more information about microbicides like the one discussed here, including fact sheets on ARV-based microbicides, please visit our download center at <http://www.global-campaign.org/download.htm>. You can also learn more about this particular study at <http://medicine.plosjournals.org>.

Final results published from CONRAD's discontinued phase III trial of cellulose sulfate

Global

As previously reported in the February 12th, 2007 issue of *GC News*, CONRAD and Family Health International (FHI) stopped their phase III effectiveness trials of the microbicide candidate cellulose sulfate (CS) when early results suggested an increased risk of HIV infection for users. At that time, the Global Campaign for Microbicides (GCM) and the African Microbicides Advocacy Group (AMAG) tried to provide advocates with what answers were available at that time from site investigators, sponsors and microbicide experts. GCM, AMAG and other HIV prevention advocacy groups also worked to counter misinformation spread by the media in the wake of the trial closures.

In the July 31st, 2008 issue of the *New England Journal of Medicine*, Dr. Lut Van Damme and her colleagues present the final analysis of data from the CONRAD trial. During the trial, conducted at three sites in Africa and two in India, 25 women using CS became infected with HIV as compared with 16 women using a placebo gel. This difference was not statistically significant, meaning that it was unclear whether the CS group with a higher number of women infected with HIV was due to using CS or some other factor. The CONRAD team was able to conclude that CS did not prevent HIV infection, and may have increased the risk of HIV acquisition. CS also showed no protective effect against two other common sexually-transmitted infections, gonorrhea and Chlamydia. Unfortunately, the researchers found no differences in self-reported rates of condoms or gel use between the treatment and placebo groups that could have explained the trend toward increased HIV infection seen with CS use.

For more information about the cellulose sulfate trials, please see <http://www.global-campaign.org/Cellulose-Sulfate.htm>.

Interpreting the PNAS article on Modeling ARV-based Microbicides

Global

Recently, various news outlets covered the release of an article, "The paradoxical effects of using antiretroviral-based microbicides to control HIV epidemics" by David Wilson et al. published in the *Proceedings of the National Academy of Sciences (PNAS)*. It describes the use of mathematical models to examine the possible implications of testing and introducing ARV-based microbicides. These news reports contained various misleading statements about the article and the study findings.

To help advocates understand and interpret the study's actual findings, we describe here the model; its limitations; and some of its predictions. We also comment on some findings in simplified terms.

How the Model Works

The article used a complicated mathematical model to explore what *might* happen if an ARV-based microbicide is made available for widespread use among women in the general population, without

additional public health interventions like regular HIV testing of microbicide users. Although the authors attempted to “model” reality, the predictive power of their model is only as good as their starting assumptions and the quality of the input data.

Modeling Drug Resistance in a Data-Sparse World – Assumptions of the model

Systemic absorption of an ARV-based microbicide

The model considers two types of microbicide candidates: those that are easily absorbed into the bloodstream and those that are not. The ones that are not easily absorbed may be less likely to result in the development of drug-resistant HIV. The authors label these different candidates “high risk” and “low risk” microbicides respectively—a confusing and problematic term because it evokes notions of high versus low risk of side effects, or high versus low risk of sexual transmission.

In theory, use of an ARV-based microbicide by an HIV-positive woman could result in drug resistance if the microbicide is absorbed into the bloodstream. However, most scientists believe that the development of drug-resistant HIV is unlikely if the microbicide is absorbed mainly into *the vaginal or rectal tissue*, with little or no drug passing in the bloodstream. The article explored mostly what might happen if a microbicide which is likely to enter the bloodstream is used. We should not discount this, but the majority of clinical studies so far do not show that this will necessarily occur.

Bi-directionality of protection

The model also looked at various levels of protective effect that the microbicide might have for the male partners of women using it. The vast majority of the model simulations described in this article were based on an assumption called bi-directional protection. This means they assumed that, if an HIV positive woman used the microbicide, it would have an effect on the HIV in her vaginal secretions and, thus, help reduce her male partners’ risk of becoming infected during sex. There is currently no evidence, however, that an ARV-based candidate microbicide (or any candidate microbicide) can offer bi-directional protection.

The Article Findings

The article emphasized a number of potential outcomes of microbicide testing and introduction that it says are “surprising.” We summarize these findings below, and argue that most of the findings are not surprising at all. In fact, they are highly predictable.

Finding 1: Few cases of drug resistant virus will likely emerge during phase III testing of ARV based microbicides because the trial protocols call for monthly HIV testing. However, resistance could emerge if the same product were widely introduced into population who are not receiving HIV testing on a regular basis.

Comment: Clinical trials of ARV-based candidate microbicides include frequent HIV testing **specifically to protect** women in the trial by limiting their chance of developing drug resistant virus. Women who seroconvert are taken off of product before resistance would likely develop. This is entirely appropriate and ethical when attempting to answer the initial question which is “does the candidate microbicide work at all?” This first question must be answered before it is possible to consider any of the subsequent questions, such as “what might happen if women who become infected continue to use the product?” It is not surprising that the model suggests that very few resistant cases will develop within the context of an effectiveness trial.

Once a product is shown to work, it will be important to evaluate the potential impact of its use by women who are HIV positive, either because they continue to use the product after becoming infected or because they begin using an ARV-based microbicide when they are already HIV positive. We will not know whether resistance is likely to develop in this context until the “next question” studies are done to find out.

Finding 2: Even a moderately effective microbicide (~50%) could have a positive effect on the epidemic by decreasing HIV transmission, if widely available and widely used. Use and adherence proved to be more important than the product's level of efficacy in preventing the greatest proportion of infections.

Comment: Although buried in the article, this is one of the article's most important findings. Similar findings have been reported by Watts and colleagues in previous modeling efforts.¹ It is also a lesson that has been demonstrated repeatedly in the family planning field. Moderately effective contraceptives that are used very consistently tend to be more effective overall than more highly effective contraceptives that are not used consistently.

Finding 3: A significant number of men could benefit from the introduction of an ARV-based microbicide.

Comment: The article placed considerable emphasis on the supposed "paradoxical" effect that a woman-initiated method could have substantial benefits for men. The potential benefit of microbicides to men, however, will depend on the degree to which the protective effect of an ARV-based microbicide is bi-directional and also how easily drug-resistant HIV is transmitted. As mentioned previously, although it is theoretically possible that a product that protects a women user would also protect her male partner, it is also possible that they won't.

The article summarized thousands of possible outcomes, each of which used different starting assumptions. Not all of these outcomes are equally likely, and the researchers did not address which combination of input assumptions might most accurately reflect reality. Consequently, the results of this modelling are a bit confusing when one is trying to draw conclusions about "real world" impact.

To view the original articles click here: <http://www.global-campaign.org/responses-articles.htm>
To view GCM's letter submitted to PNAS in response to the article click here: <http://www.global-campaign.org/clientfiles/PNAS%20LTE%20-%20Blower%20article%20-%20submitted.doc>

The Microbicides Development Programme (MDP) completes Phase III trial enrollment

Africa

The largest microbicide licensure trial to date, which is being conducted across six sites in South Africa, Tanzania, Uganda and Zambia is now closed to new participants. The Microbicides Development Programme announced on Wednesday, 20th August, 2008 that it had completed enrolment for its Phase III clinical trial of the PRO 2000/5 vaginal microbicide gel.

The full announcement can be viewed at: <http://www.mdp.mrc.ac.uk/>

Highlighted Resources

Black AIDS Institute report: *Left Behind. Black America: A Neglected Priority in the Global AIDS Epidemic.*

¹ These two studies both found that the most important factor in determining the effectiveness of an ARV-based microbicide in reducing HIV incidence is the degree of coverage and frequency of use, making access and adherence incredibly important aspects of any microbicide intervention.

North America

On July 29th, the Black AIDS Institute – a Los Angeles-based policy center dedicated to reducing HIV/AIDS health disparities in the African American community – released a new report entitled, “Left Behind. Black America: A Neglected Priority in the Global AIDS Epidemic”. African Americans comprise only one-eighth of the US population, but half of all Americans currently living with HIV/AIDS are black. More startling are the figures for African American women and youth: 60% of all cases among American women and 70% of all new diagnoses among American youth, respectively, occur within the black community. Like their counterparts in the hardest-hit regions of Africa and Asia, many black women in the US lack the tools they need to protect themselves from HIV, including the social or economic power necessary to insist on condom use or to abandon partnerships that put them at risk. The Black AIDS Institute report calls upon US policymakers and public health officials to reconsider current approaches used to address the problem of HIV/AIDS in the African American community, including education campaigns to battle myths about disease transmission, economic opportunities to empower black women, and increased research into women-initiated HIV prevention methods like vaginal microbicides and women-controlled barrier methods.

Download the full report at http://www.blackaids.org/image_uploads/article_575/08_left_behind.pdf.

The HIV Vaccines and Microbicides Resource Tracking Working Group report: Sustaining The HIV Prevention Research Agenda Global

The HIV Vaccines and Microbicides Resource Tracking Working Group generates and disseminates data on annual investments in preventive HIV vaccine and microbicide research and development, policy and advocacy activities. Their new report, launched during the IAS Mexico conference earlier this month states that although investment in the HIV prevention research and development field has increased significantly since 2000, it has stalled somewhat in 2006 and that continued funding is crucial to advancement in the field.

Total annual investment in microbicides grew from US\$65.1 million in 2000 to US\$221.9 million in 2006, however only a minimal increase of 2% was seen in 2007 to US\$226.5 million.

Download the full report at: http://www.hivresourcetracking.org/content/RT_report_August2008.pdf

For a one-page summary of the report go to:
http://www.hivresourcetracking.org/content/RT_One_Pager_2008.EN.pdf

Advocacy in Action

Spain Announces 1.5 Million Euros for Microbicide Research Europe

Amongst the hustle and bustle of the opening of the International AIDS Conference in Mexico, the Government of Spain announced its first contribution to the microbicides field. The first deputy prime minister, Maria Teresa Fernandez de la Vega announced a contribution of 10.2 million euros towards fighting HIV/AIDS around the world, of which 1.5 million is going to the International Partnership on Microbicides (the non-profit product developer focussed on producing an ARV-based, vaginal microbicide).

Fernández de la Vega has been a strong advocate for women's rights throughout her career, participating actively in the campaign to reform the abortion law in Spain. This focus on sexual and reproductive health rights for women was reflected as she expressed the need to target women in our responses to the HIV epidemic during her speech.

Spanish-based NGO Planeta Sud, a GCM partner that has been involved with advocacy at the national level in order to increase funding for HIV/AIDS and microbicides have been quoted saying "Microbicides represent a unique option for women around the world to protect their own health and safeguard themselves from HIV as never before." "Spain can be proud that we are supporting this crucial part of the global fight against HIV/AIDS. This contribution is only the latest example of Spain's commitment to improve health in the developing world, especially for women."

The contribution is welcomed by GCM.

To view the press release by IPM on the contribution visit:

http://www.ipm-microbicides.org/news_room/english/press_releases/2008/20080804_spain.htm

Conference Highlights



Microbicides at Mexico

Global

With 3 million new infections each year, the ongoing and urgent need to find women-initiated HIV prevention methods was high on the agenda at the recent International AIDS Conference in Mexico City.

Symposiums on prevention research, including 'Vaccines and Microbicides: Where do we go from here?' and 'The Future of Microbicides: From Vaginal ART to PrEP' bookended the conference. The sessions focused on moving the field forward, offering tangible next steps to address the scientific, funding and political challenges of developing new products and running large-scale trials necessary to determine if products are safe and effective.

Despite setbacks from previous results, researchers and advocates are optimistic about next-generation ARV-based microbicides. At a late-breaker session on Thursday, the Centers for Disease Control and Prevention released new data from a monkey study showing that a combination emtricitabine (FTC)/tenofovir (TFV) topical gel provided complete protection against SHIV. These exciting results support the need for further research in human clinical trials of a possible Truvada gel.

(The abstract of this session can be viewed here:

<http://www.aids2008.org/Pag/Abstracts.aspx?SID=288&AID=15936>)

As excitement about the new generation of ARV-based microbicides occupied many hallway conversations in the main Convention Centre, there was a new generation of microbicide advocates being nurtured in the neighbouring Global Village. With the field expanding rapidly, many young advocates and other new to the AIDS field were hearing the word, mi-cro-bi-cides for the very first time. For these participants, GCM offered introductory workshops in English and Spanish, including screenings of GCM's video, In Our Own Hands.

At another skills-building workshop co-sponsored by GCM, AMAG, AVAC and CHANGE, a female condom demonstration and demonstrations of microbicides applicators and rings being tested created a space for open and stark dialogue. The finger-sized applicators made the possibilities and the challenges feel real, as potential future users asked question after question about the possibility of covert use, partner involvement in studies and the practical issues around accessibility if products prove effective.

Although there are still more questions than answers, the IAC provided a virtual banquet of information, which facilitated critical conversations and exchanges and gave us all food for thought for when we return to our daily work supporting prevention research in our many corners of the world.

For webcast coverage of these sessions and more from the IAC, check out the Kaiser coverage at: <http://www.kaisernet.org/aids2008/index.cfm#guide>



No youth, no change - Young people in Mexico lead the way forward on HIV responses

Global

Addressing the sexual and reproductive health and rights of young people was high on the agenda at the Mexico Youth Force-led IAS pre-conference, with figures such as Dr. Pedro Cahn (IAS President), Peter Piot (UNAIDS) and Thoraya Obaid (UNFPA) drawing attention to the importance of ensuring that all young people, regardless of HIV status, have access to comprehensive sex education and services. The message to provide youth-friendly services, condoms and other contraceptive options as well as information about HIV in family planning clinics was welcomed by the youth advocates who travelled from all over the world to take part in the conference. Advocates were also encouraged to hear world leaders say that the innovation and creativity that only young people can provide in decision-making, policy and implementing activities must be taken on board seriously. It is only in recognising the unique understanding that young people have of the epidemic that we can move forward in new ways to address it.

The youth pre-conference involved a range of interactive skills-building sessions for young people. Arwa Meijer of the Global Campaign for Microbicides joined a team of young people who presented a session on 'Expanding prevention options for women and girls'. Throughout the session, youth advocates raised complex and considered questions demonstrating how gender, sexuality and exclusion can impact on young people's vulnerability to HIV. These issues were discussed and the session explored how the role of existing and new prevention technologies can work to promote the sexual and reproductive health rights of young people. There was much enthusiasm amongst young leaders to advocate for the scale-up of female condoms and for research and development into new prevention technologies such as

microbicides, PREP and vaccines that help to bridge the gap of inequality faced by young women and girls.

The pre-conference ended on a high note with young people taking part in the 1st International March Against Stigma, Discrimination and Homophobia. The cries of 'No hay libertad politica si no hay libertad sexual' (No sexual liberty equals no political liberty) resonated strongly with youth advocates and set the tone for the main conference where young people called for more comprehensive HIV prevention strategies and for strong leadership and commitment to youth issues to be sustained over time.