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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 Updates

Carraguard trial results expected in mid February

South Africa

Shortly after this issue of *GC News* goes to press, the results of the first large-scale effectiveness trial of a novel microbicide to reach completion are expected to be announced. From 2004 to 2007, the Population Council, with funding from the US Agency for International Development and the Bill and Melinda Gates Foundation, conducted a phase 3 trial to measure the effectiveness of Carraguard® to prevent heterosexual acquisition of HIV by women.

The active ingredient in Carraguard is carrageenan, a natural substance found in seaweed that may provide a physical barrier that protects the vulnerable cells of the vagina and cervix from HIV and other sexually-transmitted diseases. Over 6,000 women in South Africa volunteered to be part of this clinical trial, in which participants were randomly assigned to either receive Carraguard or a comparator gel that did not contain carrageenan. Trial participants were instructed to use the gel plus condoms every time they had sex, and asked to return to the study clinic repeatedly over a two-year period. During this time, they were provided with condoms and received comprehensive risk reduction counseling, HIV testing, and screening and treatment for STIs.

Although the results of the trial are not yet known, the fact that the trial reached completion is itself a breakthrough. Successful completion of the Carraguard trial is a testament not only to the commitment of the study investigators but also to the dedication of the trial participants themselves. Regardless of the results, this trial will yield important information about microbicide effectiveness, safety, use, and acceptability, and will help researchers design and test new HIV prevention technologies.

The Global Campaign for Microbicides will send out a special alert to all *GC News* subscribers once the final results of the trial are released. Until then, you can learn more about the Carraguard trial by visiting http://www.global-campaign.org/carraguard.htm

HSV-2 treatment does not reduce the risk of HIV infection

Global

Herpes simplex virus 2 (HSV-2), the virus that causes genital herpes, is one of the most common sexually-transmitted infections in the world. Infection with HSV-2 increases an individual's risk of acquiring HIV. The risk of becoming HIV infected is three times higher among heterosexual men and women with genital herpes and almost twice as high among MSM. This observation led researchers to wonder if suppressing HSV-2 with an antiviral drug like acyclovir might help reduce the risk of HIV infection among those with genital herpes.

The HIV Prevention Trials Network (HPTN) recently undertook a large randomized, placebo-controlled study to test this hypothesis. The trial, known as HPTN 039, enrolled 3,251 HIV negative participants who had genital herpes and were at risk of acquiring HIV sexually. MSM from the United States and Peru made up about half (1,871) of the participants, and the other half (1,380) were heterosexual women in South Africa, Zambia and Zimbabwe. Participants were randomised to receive either 400 mg acyclovir twice daily or placebo pills. They were then followed for 12 to 18 months, with quarterly HIV tests and monthly visits to provide additional risk-reduction counseling and to monitor drug adherence.

Unfortunately, the preliminary results (presented at the recent Conference on Retroviruses and Opportunistic Infections in Boston) suggest that this intervention is not effective in reducing the risk of HIV acquisition. Seventy-five new HIV infections occurred among the trial participants receiving acyclovir and 64 new HIV infections among trial participants in the placebo group. Although there were 11 more seroconversions in the acyclovir versus placebo group, this difference was statistically insignificant and likely due to selection bias or chance.

This was surprising given that only 5% of participants reported that they did not take their pills on schedule and that the number of HSV-induced genital ulcers reported by participants or seen during exams was 35% lower in the acyclovir versus placebo group.

As disappointing as these results are, the HPTN 039 study did demonstrate that wide-scale treatment of genital herpes is achievable and sustainable even in resource-poor countries. Since HIV is frequently shed from the genital ulcers caused by herpes, acyclovir treatment to prevent them might yet be a useful tool for preventing HIV transmission. Treating HIV-positive people who have genital herpes with acyclovir might reduce their viral shedding and thus help protect their partners from exposure to HIV, but additional research is needed.

The Global Campaign for Microbicides will continue to monitor the results of this and similar STI treatment trials and will update you regularly as new information arises. For more information about this and other trials of novel HIV prevention technologies, please see http://www.global-campaign.org/. You can also learn more about the HTPN 039 study at http://www.hptn.org/research_studies/hptn039.asp.

Benefits of adult male circumcision limited to heterosexual men

Global

Several widely publicized studies have shown that adult circumcision of men reduces significantly their risk of acquiring HIV heterosexually. Circumcised men are 40 - 60% less likely to acquire HIV from an infected female partner. UNAIDS and the World Health Organization are now promoting male circumcision as part of a comprehensive prevention package to prevent heterosexual transmission of HIV, in addition to voluntary counseling and testing, education in safe sex practices and the use of condoms, and treatment of sexually transmitted infections (STIs). Until now, however, it has been unclear if adult male circumcision would also protect male and female receptive sex partners. Unfortunately, two recent studies suggest that it may not.

A trial that followed 161 serodiscordant married couples in Uganda (couples in which the husband was HIV positive and the wife was negative) produced data suggesting the female partners of recently circumcised HIV-positive men were at heightened risk of infection if the couple resumed sex before the circumcision wound is fully healed. All participants in the trial were offered free condoms and were provided comprehensive risk reduction counseling, HIV testing, and screening and treatment for STIs.

Although circumcision helped to lower the men's incidence of herpes and genital ulcers, the study found that circumcising HIV-infected men did not protect their wives from HIV or other STIs. In fact, the women appeared to be at heightened risk of HIV infection if the couple resumed sex before the circumcision wound was fully healed. During the first six months of follow-up, 28.8% of the women partnered with men who resumed sex prior to certified wound healing became infected with HIV. By contrast, only 9.5% of the wives of men who resumed sex after certified wound healing and 8.8% of the wives of uncircumcised men seroconverted during the follow-up period.

Overall, there was no statistically significant difference in the rate of HIV infection among the wives of men who were circumcised versus women whose husbands were not circumcised. It is possible that wide-scale roll out of adult male circumcision may have a positive but indirect effect for women in the long run by lowering the overall rate of HIV incidence among men in the general population. However, there is no evidence of an immediate, protective benefit for individual women in high-risk communities.

Similarly, a recent study published in the December 15, 2007 issue of the *Journal of Acquired Immune Deficiencies Syndromes* compared circumcision status and HIV infection among 1,154 black and 1,091 Latino men who have sex with men (MSM) in New York, Philadelphia and Los Angeles. Previous studies looking at circumcision and HIV infection in MSM failed to include large numbers of black and Latino men, who are disproportionately affected by HIV in the United States and are less likely to be circumcised than Caucasians. In this latest study, no association between circumcision status and HIV infection was seen, suggesting that circumcision is not associated with reduced risk of HIV infection among men who have sex with men.

For more information about male circumcision as an HIV prevention option, visit http://www.globalcampaign.org/malecircumcision.htm.

Science Bites: Biomedical and social science advances in HIV prevention

Global

1. Another candidate is added to the microbicide development pipeline

As reported in the January 30, 2008 issue of the *Wall Street Journal*, the pharmaceutical company Pfizer has agreed to license its new antiretroviral drug Selzentry™ to the International Partnership for Microbicides (IPM) for development as a topical vaginal microbicide. Generically known as maraviroc, Selzentry is currently the only US FDA-approved drug belonging to a new class of compounds called CCR5 antagonists. CCR5 antagonists work by blocking a protein on the surface of cells called CCR5, which certain strains of HIV use to enter and infect target cells. Although a lot of work still needs to be done before a Selzentry-based microbicide will be ready for testing, Pfizer's decision to license maraviroc for development as a microbicide adds one more promising candidate to the microbicide development pipeline.

2. Swiss experts purport people with undetectable viral loads and no STI cannot transmit HIV

The Swiss Federal Commission for HIV/AIDS recently issued a statement concluding that, "an HIV-infected person on antiretroviral therapy with completely suppressed viraemia ("effective ART") is not sexually infectious, i.e. cannot transmit HIV through sexual contact." This conclusion took many experts by surprise, and has caused consternation among HIV prevention researchers and advocates alike.

The Global Campaign for Microbicides is concerned that the Swiss Commission's statement sends a risky message for the following reasons:

- We know that far too few HIV-infected individuals in hard-hit regions around the world have access to cutting-edge treatment, and far fewer have access to viral load monitoring. Thus, the desire to view oneself as "not sexually infectious" may far outstrip people's ability to know for a fact that their viral load is undetectable.

- We also know that undiagnosed and untreated STIs are epidemic worldwide and that these infections increase both the risk of acquiring and the risk of transmitting HIV.

- Work by researchers like Dr. Andrea Kovacs from the Women's Interagency HIV Study has demonstrated that a significant number of women with undetectable viral loads in their blood nevertheless have detectable levels of virus in their vaginal secretions (*Lancet* 358: 1593-601). Undetectable virus in one part of the body doesn't mean undetectable everywhere in the body.

Advances in antiretroviral treatment have greatly improved the health and wellbeing of those living with HIV/AIDS, and treatment interventions hold great promise for reducing the risk of transmitting HIV. Nevertheless, it is premature to promote the message that HIV-infected persons on treatment can forego safe sex practices without putting their sexual partners at risk.

3. Animal studies provide supporting evidence for pre-exposure prophylaxis

In a study recently published in the open-access journal *PLoS Medicine* (5: e28. doi:10.3171/journal.pmed. 0050028), researchers at the US Centers for Disease Control (CDC) found that treating macaques with daily or intermittent doses of the antiretroviral drugs tenofovir and emtricitabine prior to weekly repeated rectal exposure to a humanized version of simian immunodeficiency virus delayed or prevented viral infection in a majority of monkeys. Although pre-exposure prophylaxis (PrEP) has yet to be shown to prevent sexual transmission of HIV in humans, the results of this and previous animal studies provide proof-of-concept (i.e. PrEP can protect people at risk of HIV). The results of the CDC study also suggest that PrEP may work even if persons at risk of acquiring HIV only take their antiretroviral drugs around the time of exposure rather than daily.

It must be re-emphasized, however, that there is no proof that PrEP will work for humans. As several microbicide trials have already shown, drugs that are safe and effective for animals do not always prevent humans from acquiring HIV. In the absence of clinical trials, it would be dangerous to assume that intermittent use of PrEP in humans (or "disco-dosing" as it is sometimes called) has any effectiveness at all.

Advocacy in Action

"Missing chapter" on civil society added to the *Microbicide Development Strategy*

Global

In 2005, the Microbicide Donors' Committee—representing 14 funding agencies and governments currently supporting microbicide research—spearheaded the creation of the *Microbicide Development Strategy* (*MDS*) as a framework for prioritising decisions made by funders, researchers and developers. Developed by four working groups, the MDS laid out a strategic framework for action in four areas: 1) basic and pre-clinical science; 2) clinical research; 3) manufacturing and formulation; and 4) commercialization and access.

At the first draft review of the *Microbicide Development Strategy* in late 2005, the Global Campaign for Microbicides, among others, expressed concern about the fact that civil society involvement and advocacy were not explicitly included in the analysis. To remedy this, GCM convened a Civil Society Working Group to craft a comparable framework for civil society involvement in the field.

The Working Group's 11 members represent a cross-section of professional backgrounds, geographic representation, and spheres of influence (i.e., local, national, regional, and international). As researchers, advocates,

program planners and managers, and health care practitioners, all work at the intersection of research and advocacy, or research and program implementation and are connected to large networks of advocates in their local regions.

The Working Group pinpointed dozens of gaps that need attention but chose to focus its analysis specifically on the seven issues that were both of greatest concern to civil society and that, if addressed with targeted investments of energy and resources, could result in immediate benefit to the field. It then identified seven priority actions needed to address those gaps and broke down those actions down into 55 interlocking implementation steps—concrete activities that, if undertaken, should generate real progress toward the goal of assuring full civil society integration into the field at all levels.

After over a year of deliberations and drafting, the Working Group's report will be launched at the Microbicides 2008 conference. Entitled "*The First 55 Steps: A Report of the Microbicide Development Strategy's Civil Society Working Group*", the report:

1. Provides an overview of the status of civil society engagement in each phase of microbicide research, development and introduction; and
2. Identifies the resources and specific action steps needed to move from the current level of engagement (which is minimal, scatter-shot and under-resourced) to where we need to be (with civil society engaging as a full partner).

The report also offers a detailed view of the essential and positive contributions that civil society can and should play across the whole arc of the microbicide research and development process.

Commissioned as the "missing chapter" of the *MDS* (and accepted as such by the *MDS* authors as such), this report lays out concrete, feasible, and pragmatic steps for moving forward. We hope that, like the *MDS* itself, it highlights for funders, researchers, developers and advocates, the action and investments required to achieve efficiency, accountability and optimal synergy in the field.

The members of the Microbicide Development Strategy Civil Society Working Group were:

Susan Chong, MA (Southeast Asian Studies), Asian/Pacific Coalition of AIDS Service Organisations, Malaysia
Janet Frohlich, PhD, Centre for the AIDS Programme of Research in South Africa (CAPRISA), South Africa
Miriam Katende, The AIDS Service Organisation (TASO), Uganda
Alex Menezes, International AIDS Vaccine Initiative (IAVI), Brazil
Dr. Chidi Nweneka, Pro-Hope International, The Gambia
Dr. Sai Subhasree Raghavan, Solidarity & Action Against The HIV Infection in India (SAATHII), India
Seema Sahay, PhD, National AIDS Research Institute (NARI), India
Laurie Sylla, MHSA, Yale AIDS Program, USA
Dr. Morenike Ukpong, Nigeria HIV Vaccine and Microbicide Advocacy Group (NHVMAG), Nigeria
Sydney West, Global Campaign for Microbicides, USA
Lydia Zigomo, Interact Worldwide, UK

The report, written by Global Campaign staffer Anna Forbes, Laurie Sylla, and consultant Rachel Yassky, and the executive summary are available online at http://www.global-campaign.org/mds.htm.

Rectal microbicide advocates call for five-fold funding increase

Global

International Rectal Microbicide Advocates (IRMA), a global network of over 500 advocates, policy-makers, and leading scientists from 40 countries on six continents, will release *Less Silence, More Science: Advocacy to Make Rectal Microbicides a Reality* at this month's Microbicides 2008 conference. The report, to be presented on Monday, February 25, 2008 as part of the Conference's panel discussion on rectal microbicides, serves as an authoritative reference on recent developments and current efforts in rectal microbicide research, and describes global challenges, key advocacy goals, strategies and activities of IRMA.

The report calls attention to the fact that anal intercourse among gay men and other men who have sex with men, as well as between women and men, is an important driver of the HIV pandemic in many parts of the world. According to IRMA, one of the dangerous silences of global HIV prevention efforts has been the neglect "of anal intercourse between women and men as well as the HIV prevalence among, and indeed, the mere existence of, gay men and other men who have sex with men in Asia, Africa and other parts of the developing world. This neglect costs lives."

Globally, most anal intercourse is unprotected and new prevention technologies like rectal microbicides are needed. Currently in development, rectal microbicides are products that could be used to reduce a person's risk of HIV infection through anal intercourse in the absence of condoms, and would provide additional protection with condoms.

Research into rectal microbicides, as described in the IRMA report, is more robust than it has ever been, but these efforts are hampered by a deplorable lack of funding. In 2006, only US$7 million/year was invested globally in rectal microbicides research. It is estimated that it will require an investment of at least US$350 million over the next 10 to 15 years, or roughly US$35 million a year, to develop a comprehensive research program. Thus, annual spending must increase five-fold to ensure timely discovery and development of a rectal microbicide.

Less Silence, More Science also provides a glimpse at the results from the world's largest survey on anal sex, conducted last year by IRMA. The web-based survey gathered data on the types of lubricants people use for anal sex, as well as preferred lube characteristics, from almost 9,000 people from 107 countries.

The lubricant survey showed that a rectal microbicide formulated as a lubricant would be an ideal way to provide protection to those who engage in anal intercourse. Indeed, a rectal microbicide formulated as a lube would probably be highly acceptable, especially if it has no flavour, colour or smell, and is available in both thick and liquid consistencies as either a water or silicone base.

Beginning February 25, 2008, the full report will be available for download from IRMA's new web site (http://www.rectalmicrobicides.org).

Victory for the *Unproven Product Claims Watch*: Kirklees Medical Limited
United Kingdom

Since 2002, the Global Campaign for Microbicides has maintained an Unproven Product Claims Watch to raise public awareness of products that are promoted as effective microbicides without substantiating evidence and to advocate for the removal of such products from the market wherever possible.

As reported in Issue 86 of *GC News*, GCM has been working with the International Rectal Microbicides Advocates (IRMA), Terrence Higgins Trust (in the UK), SENSOA (in Belgium) and other allies to investigate the claims of Kirklees Medical Limited, a UK-based lubricant manufacturer. Kirklees had made explicit advertising claims on their website and on other Internet sites regarding the ability of its K-Lube products to reduce HIV risk. In response, Kirklees Medical has now removed all misleading advertising claims from its website. As Jo Robinson of the Terrence Higgins Trust reports, "we're really pleased to report that, having worked in partnership with the [UK] regulator, Kirklees Medical Ltd [has] now removed any ambiguous and misleading comments from their website. Now gay men and other customers can access simple factual and accurate information about their range of lubricants and sexual health information, which is a great result all round. For microbicide advocates in the UK and elsewhere it is also encouraging and shows that if you are patient and trust in the process you can work with great success with the regulatory authorities to challenge companies that make false claim."

Highlighted Resources

F-SPOT India

The Global Campaign for Microbicides is pleased to announce the launch of a new moderated listserv focusing on microbicides and other HIV prevention technologies in India. Called Female STI/HIV Prevention Options Today (F-SPOT) India, this listserv provides a forum for advocates, researchers, and community members to: 1) share information on female-initiated HIV prevention technologies, with a particular emphasis on microbicide research, development, introduction, and access; and 2) create an electronic platform for dialogue amongst different stakeholders on HIV prevention-related issues. To learn more about F-SPOT or to join the discussion, please email the moderator Paramita Kundu at pkundu@path.org.

New report: Advocates' consultation on Carraguard and VOICE study

As we previously reported in issue 88 of *GC News*, on 18-19 October 2007, the Microbicide Trials Network (MTN) and the Population Council sponsored an advocates' consultation on the Carraguard and VOICE studies in Johannesburg, South Africa. Convened by the African Microbicides Advocacy Group (AMAG), African Rights and Alliance for Southern Africa (ARASA), AIDS Vaccine Advocacy Coalition (AVAC) and the Global Campaign for Microbicides (GCM), the meeting provided the opportunity for 25 African advocates to review the status of microbicides and pre-exposure prophylaxis research internationally and discuss issues in prevention trials from an advocacy perspective.

A summary report of the meeting and the key issues, recommendations and action items it elicited is now available. To access the full report, go to http://www.global-campaign.org/clientfiles/AdvocatesConsultationReport18-19Oct2007.pdf.

Participants in the Advocates' Consultation on HIV Prevention Trials (clockwise from bottom left):

Margaret Muganwa (SWAA International/Uganda), Cecelia Mhiti (Southern Africa AIDS Information Dissemination, Zimbabwe), Anna Forbes (GCM), Anna-Colletor Penduka (Women's AIDS Support Network, Zimbabwe) and Clementine Mumba (Treatment Action and Literacy Campaign, Zambia).

Conference Highlights

Microbicides 2008

India

The biannual Microbicides 2008 Conference will be held from 24-27 February 2008, at the Hotel Ashok in New Delhi, India. The Global Campaign for Microbicides invites you to join us for the following activities:

1. M2008 Pre-Conference Workshop

The Global Campaign for Microbicides, the African Microbicides Advocacy Group (AMAG), the Indian Network of NGO's (INN), the National Coalition on Health Initiatives (NCHI) and the Positive Women's Network (PWN+) are hosting a Pre-Conference Workshop on Sunday, 24 February 2008, preceding the formal opening of the Microbicides 2008 Conference at 17:30.

The Microbicides Pre-Conference Workshop is designed to provide advocates with an introduction to some key topics in the microbicide field, to allow for discussion between and among community advocates and researchers, and to prepare participants to fully engage in the discussions that will take place in the coming week at the conference. The pre-conference workshop will also provide the opportunity for those new to the

microbicides field to learn and/or review some of the microbicide basics in our Microbicides Basics breakout session.

The Pre-Conference Workshop will be held on Sunday, February 24, 2008, from 09:00 – 15:00 at the India Habitat Centre (IHC), Lohdi Road, New Delhi. Participants are being asked to take taxis from their hotels to the IHC for the pre-conference event. The IHC is very well known in Delhi and taxi drivers should be familiar with its location. GCM will provide transportation reimbursements of up to 500 INR to cover the cost. Reimbursements will be given at check-in. Morning traffic in New Delhi can be very unpredictable. Because of this we are asking participants to please leave their hotels by 08:00 to reach the IHC in time, check-in and collect their reimbursements. After the conclusion of the Pre-Conference, GCM will provide buses to transport participants from the IHC to the Ashok Hotel for the opening ceremony of the M2008 Conference.

There is no registration fee for the Pre-Conference workshop and registration for the M2008 Conference is not a requirement for participation. For more information on the workshop, please visit http://global-campaign.org/M2008.htm.

2. Advocate's Corner

During the duration of the Microbicides 2008 conference, the Global Campaign for Microbicides, the African Microbicides Advocacy Group (AMAG), Indian Network of NGOs (INN) Gujarat, International Rectal Microbicides Advocates (IRMA), National Health Coalition Initiatives (NHCI), and Nigerian HIV Vaccine & Microbicide Advocacy Group (NHVMAG) will be hosting an Advocates' Corner.

Located in the M2008 Exhibition Hall, the Advocate's Corner is an interactive and participatory area where M2008 conference delegates representing community, advocacy and civil society groups can come to talk, exchange ideas, network, and build solidarity. The Advocate's Corner will also host a number of activities that delegates are invited to attend, and will provide a "chill-out space" at which conference participants can relax in-between official conference sessions. Advocates will be able to pick-up a schedule of events, sign up for skills building and informational sessions, and reserve a time to use the space for their own purposes. The "Corner" will also offer a wide range of materials from various organisations that advocates can use in their work back home.

For more information on the Advocate's Corner, please visit http://global-campaign.org/M2008.htm.

We welcome your input and contributions for future issues! Please send emails to: info@global-campaign.org. If you would like to unsubscribe to the *Global Campaign News*, please reply to this e-mail with the subject line: UNSUBSCRIBE