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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 STIs. This and previous issues of *GC News* are available online at http://www.global-campaign.org/gcnews.htm

In this issue:

Trials Watch

Looking back at trial closures over the past year

Africa

In the past two years, six important HIV prevention trials—two in Nigeria and one each in Cambodia, Cameroon, Ghana, and Malawi--have been shut down early, stopped before they began, or shifted enrollment to new sites. While all the trials were attempting to evaluate the effectiveness of either microbicides or oral tenofovir as pre-exposure prophylaxis (PREP), it is important to recognize that they were discontinued for very different reasons.

SAVVY GHANA TRIAL
In November 2005, Family Health International (FHI) and Cellegy Pharmaceuticals announced plans to discontinue an on-going Phase III study of the effectiveness of Savvy, a candidate microbicide.

In the Savvy Ghana trial, HIV incidence in the study population was too low to show whether use of Savvy, compared with a placebo gel, would prevent HIV. It was deemed impossible to expand or extend recruitment sufficiently at the Ghana sites to make up for the lower than expected incidence. There were just not enough eligible women in these settings to make expansion feasible.

The relatively low overall incidence suggested that condom counseling, HIV testing, and other prevention interventions provided to participants may have contributed to a reduction in the number of HIV infections. These findings represent a public health success, but such low incidence meant that the study could no longer answer the question about product effectiveness.

SAVVY NIGERIA TRIAL

Almost a year later in September 2006, FHI and Cellegy announced the premature closure of a second Savvy trial, this one taking place in Nigeria. While HIV incidence in the study population was also lower than anticipated, the decision to close this study had a different rationale. The independent Data Monitoring Committee (DMC) recommended discontinuing the study because interim review of the unblinded data suggested that there was no evidence that Savvy was reducing risk of HIV transmission. If they had found evidence of a protective effect, investigators could have extended the trial and enrolled more women in order to compensate for the lower than expected incidence rate. In both studies the rates of side effects were similar between the product and placebo groups, and study participants experienced no serious medical problems deemed related to product use.

To date, nearly 70 percent of the women in the Savvy Nigeria study currently in follow-up have completed all their planned visits. The FHI study team plans to inform each woman who has not already completed the study about the study closure at her next scheduled follow-up visit, when she will receive a final HIV test. In short, they will follow the same, standard study procedures that were used with participants who have already completed the study. These procedures have been reviewed and approved by the local ethical review committee and Nigeria's national drug agency, the National Agency for Food, Drug Administration and Control (NAFDAC).

The study clinics will remain open until 15 December 2006 so that study participants can come in for additional counseling, information, test results, and condoms. Once all the remaining follow-up visits have been completed, FHI will analyze the data and report the study results to the local and international community.

The site investigators have written agreements in place with the local PEPFAR programs to provide care to participants who tested HIV-positive during the study, including antiretroviral treatment as needed.

Given that these two large studies failed to provide even preliminary evidence of Savvy's effectiveness against HIV, it is unlikely that sponsors will pursue further research on Savvy as a potential microbicide. Other organizations are continuing to conduct trials in the United States to determine if Savvy is effective as a contraceptive.

CELLULOSE SULFATE NIGERIA TRIAL

This month FHI, CONRAD and USAID made a joint study management decision to expand their Phase 3 trial of cellulose sulfate to a second country in sub-Saharan Africa while ending recruitment of new participants in Nigeria. Follow-up will be completed in Nigeria for the nearly 1,600 women already enrolled in the study.

This decision was made after a review by the study's independent DMC, conducted on 5 September, found that no serious symptoms or medical conditions were associated with gel use, leading to the DMC recommendation to continue the trial. In this case the interim analysis examined only safety data, as required by the study protocol, and not effectiveness data.

This trial was designed to enroll over 2,100 Nigerian women at sites in Lagos and Port Harcourt. At trial initiation, the anticipated HIV incidence in this population was 3.75 percent. By August 2006, with about 70 percent of planned enrollment completed, overall annual HIV incidence among study participants was less than 2 percent. Lower-than-anticipated incidence means that the size of the study needs to increase to ensure that results will be statistically significant. Based in part on instability in the oil-producing Delta region of the country, where one of the research sites is located, FHI determined that the most efficient way to complete the study was to expand to another site with high HIV incidence outside of Nigeria.

As the study continues in Nigeria, any women who seroconvert will continue to be referred to PEPFAR programs in Lagos or government-subsidized programs in Port Harcourt that have agreed to provide them care and antiretroviral treatment when needed. A written agreement is also in place with the PEPFAR centers in Lagos to provide these services free of charge to participants from Port Harcourt if they are willing to relocate.

A similar (but separate) study of cellulose sulfate is continuing in Benin, Burkina Faso, India, South Africa, and Uganda sponsored by CONRAD.

ORAL TENOFOVIR TRIALS

As described in previous issues of GC News, four other trials evaluating once-a-day use of tenofovir for oral prophylaxis have also been suspended in the last 2 years – Cambodia, Cameroon, Malawi and Nigeria. Again the reasons behind these closures vary by site. The Cambodian and Cameroonian studies were both subject to intense media criticism and controversy due to ethical concerns raised by activist groups. These closures were due to unresolved controversy. By contrast, the Nigerian trial of oral tenofovir did not close due to protest, but because of data irregularities and other technical problems. The Malawi study was suspended before it began because concerns were raised that the use of tenofovir for oral prevention might undermine its utility as an HIV treatment drug.

In Nigeria, the women who became infected during the trial were referred to PEPFAR programs for care and treatment. In Cameroon, study staff offered those who seroconverted referrals to, and assistance accessing if needed, HIV-related psychological, social and medical services in their communities. These services include tenofovir resistance, viral load and CD4 level testing and antiretroviral drug provision when indicated. In both Malawi and Cambodia, no women serocoverted because the trials never began enrolling.

FHI releases combined preliminary results from several oral Tenofovir studies
Global

Tenofovir--well-known in HIV/AIDS treatment circles--has been used for years as one of many treatment options for those living with HIV/AIDS. The drug has received increased attention recently as researchers have worked to expand its use from HIV treatment to HIV prevention. The hope is that tenofovir could help reduce the risk of acquiring HIV if taken once a day as a "prevention pill" –a strategy known as pre-exposure prophylaxsis (PREP).

As discussed above, the attention given to tenofovir has not always been positive, however. Most notably, two oral tenofovir trials, one in Cameroon and one in Cambodia, came under harsh criticism from the media and activists due in part to inaccurate press coverage and unresolved issues around standard of care for trial participants. The Cambodian trial was suspended before it formally began in August 2004 and the Cameroon trial was shutdown in 2005. Nonetheless, researchers and advocates have re-committed themselves to working together to ensure the ethical and safe completion of future PREP trials.

At the 16th International AIDS Conference in Toronto last month, Family Health International (FHI) released preliminary findings from the combined results of the oral tenofovir studies they conducted in Ghana, Nigeria and Cameroon. Because the Nigerian and Cameroonian studies were closed early, and because the trials experienced lower than expected HIV incidence, there were too few HIV infections to draw conclusions regarding the effectiveness of tenofovir for oral prevention. Nonetheless, the combined data demonstrated that oral tenofovir (or Viread as it is manufactured and marketed by Gilead) appeared safe and was generally well tolerated. Importantly, there were no significant differences in liver or kidney functioning between individuals who received tenofovir and those who received a placebo.

Overall HIV infections occurred in two women taking Viread, and in six women taking the placebo. But scientists warn that given the small number of infections involved, these findings should not be over-interpreted. As lead investigator, Dr. Ward Cates of FHI observed in the Wall Street Journal, "Because the numbers were low, we could have observed this [infection rate] by chance. It's important that we have additional studies to determine if it is effective and, if so, how effective".

Additional studies are currently underway with funding from the U.S. Centers for Disease Control & Prevention (CDC) and the National Institutes of Health (NIH) to determine whether tenofovir (or other PREP regimens) will be effective in preventing the transmission of HIV. CDC studies are planned or underway in Thailand, Botswana and the U.S., and a NIH sponsored study will soon begin enrolling MSM in Peru.

Advocacy in Action

Advocates demand full funding for the Microbicides Trials Network
North America

On 15 September, 117 non-governmental organizations (NGOs) sent a letter to Dr. Elias Zerhouni, the director of the U.S. National Institutes of Health, demanding full funding for the newly launched Microbicides Trials Network. In an effort spearheaded by the Global Campaign and supported by partners around the country, NGOs banded together in a period of only one week to demonstrate broad-based support. The signatories included a diverse group from the Committee of Ten Thousand, ACT UP, and the Streetworks Project to the AIDS Vaccine Advocacy Coalition, Planned Parenthood and the Visiting Nurses Association of Potts County, Iowa. We will keep GC News readers posted of any response that is received. Excerpts from the letter are included below, and you can view the full letter and list of signatories at *www.global-campaign.org/GCNorthAmerica.htm*.

Excerpts:
"In the wake of the 16th International AIDS Conference, and in light of the many strong statements made by senior policymakers and scientists in support of an accelerated global effort to develop microbicides, we are alarmed to learn that US support for microbicide research has not expanded to meet the needs of this powerful new HIV prevention technology.

"…We, the undersigned, understand that NIH is experiencing a flat budget. It is not reasonable, however, to expect the MTN to complete its ongoing trials and to deliver new studies on $15.9 million in Year 1 – barely two-thirds of the $22.3 million it projects is needed to cover its program of work.

"…We are united in advocating for a broad spectrum of federally-funded work that includes the creation of new HIV prevention options such as vaccines and microbicides, as well as the uncompromised maintenance of existing prevention, care, treatment, and support services. Treatment and prevention are inseparable goals and we were all encouraged by the long-overdue commitments articulated in Toronto to prevention in general and microbicides in particular. But this commitment is only empty words if the reality is that the MTN is funded at a level that necessitates the elimination of essential functions. Such empty rhetoric is wholly unacceptable to all of us.

"As civil society representatives, we are specifically concerned that the MTN's proposed mechanisms to assure adequate civil society and community involvement in the trials may not be implemented at this reduced funding level.

"The Microbicide Trials Network cannot realize its promise at the reduced budget allocation We, therefore, urge you in the strongest possible terms to secure a level of funding sufficient to implement the MTN's work plan as designed.

"Microbicide research and development have been under-funded and, as a result, progress in the field has been delayed for far too long. The price of this delay is paid in human lives. It is absolutely essential that we get safe, effective microbicides into the hands of all who need them as rapidly as possible. There can be no excuse for underfunding such a global objective or for the US National Institutes of Health to falter where its leadership could be so critical."

Mobilising African communities living in the UK to support microbicide research

Europe and Africa

On 3 August, representatives of the National Health Service and nine UK NGOs dedicated to HIV prevention and treatment efforts with African communities came together in London to discuss how they can mobilise greater support for microbicides in the UK. Jointly organised by the UK African Working Group on Microbicides and the Global Campaign, the half-day meeting focused on building the capacity and confidence of the participants to advocate for microbicides with their constituencies and communities.

The workshop began by identifying the specific problems that face African microbicide advocates, including the provision of scientific and technical detail and concerns around microbicides access. A key topic was the fear of exploitation in clinical trials and the importance of equality in global research efforts. In an interactive discussion, participants explored the myths and misperceptions that surround trials and gained confidence in answering questions about the science and ethics of microbicide development.

The meeting ended with a discussion on ideas for next steps for the African Working Group, which meets quarterly as part of the UK Campaign for Microbicides. For the copy of the report, please click here: *http://www.global-campaign.org/clientfiles/TrainTheTrainerReport.pdf*

Launch of Chicago Coalition for Microbicides

North America

After years of conducting local outreach with partner groups, this summer, the AIDS Foundation of Chicago (AFC) brought together HIV/AIDS and women's reproductive health advocates, sex educators, harm reduction specialists, violence prevention advocates, and others in a more formal coalition to advance microbicides advocacy and education in Chicago. This newly formed citywide partnership, known as the Chicago Coalition for Microbicides (CCM), is taking decisive action to inform and mobilize their diverse constituencies. Member organizations are already integrating microbicides into their present work in a number of creative ways. For instance, African American Women Evolving will feature a session on microbicides at their annual conference in the fall. The Battered Women's Network's domestic violence advocate training manual will now include information about how microbicides could be used as part of safety planning, once they become available. Feminist-owned sex shop Early to Bed is distributing informational post cards to all customers. The Chicago Foundation for Women is organizing a panel on microbicides for the fall, featuring Dr. Sharon Hillier. The Chicago Women's AIDS Project is leading organizations on Chicago's south side in an event featuring the display the *Giving Women Power Over AIDS* exhibit for January of 2007. Other partners are providing staff trainings on what microbicides are and the role they could play in the lives of the communities with which they work.

This November 15, the Chicago Coalition for Microbicides will host an extensive training for advocates conducted by the Global Campaign's very own Bindiya Patel. Interested individuals should contact Jessica Terlikowski at *jterlikowski@aidschicago.org* for more information.

New York Working Group helps launch *Mehret* – a documentary in progress

North America

On 7 September, Pureland Pictures along with several sponsors hosted a party at a club in Brooklyn featuring a trailer for their feature length documentary on women and AIDS – *Mehret*. The documentary follows Dr. Mehret Mandefro, who treats HIV-positive patients in the South Bronx and Ethiopia (her birthplace) as she tries to understand why love and sex are a life-and-death struggle for the black women she sees everyday. Mehret's mission takes her to the new front-lines of the AIDS crisis where she uncovers what most women don't say about intimate relationships and the deadly risk of that silence. The film aims to:

- Raise awareness about black women's special vulnerability to AIDS and
- Create awareness about the private power struggle women across boundaries of race, class and culture face in the bedroom.
- Demonstrate the need for woman-controlled prevention methods
- Inspire and inform activists and public health professionals
- Be a tool for organizations worldwide already mobilizing to combat HIV/AIDS among women and girls

The New York Microbicides Working Group and the Global Campaign for Microbicides worked with the film-makers to include the *Giving Women Power Over AIDS* exhibit at the party. With 355 people attending the party, the event raised over $6,000 toward post-production of *Mehret*.

The film-makers will be hosting events in Boston, Chicago, San Francisco, and Philadelphia in the coming months. For more information about the film, visit *www.purelandpictures.com* and get in touch with *info@global-campaign.org* if you're interested in working in your city to help support their efforts.

Global Campaign welcomes new program assistant to our DC office!

North America

The Global Campaign secretariat is pleased to announce the newest addition to our team. Jui Shah will be working in the D.C. office to support the entire secretariat team and help manage our information resources. Prior to joining

the Campaign, Jui held internships at the American Cancer Society and the Reproductive Health Technologies Project. She also spent a summer running HIV/AIDS education programs in Malawi with Operation Crossroads Africa and studied abroad at Universidad de Sevilla in southern Spain. Jui earned a Bachelors degree in Foreign Service from Georgetown University. You can contact Jui for materials or other GCM needs at jshah@path.org.

New Resources

AVAC Report 2006: AIDS Vaccines: The Next Frontiers

The AIDS Vaccine Advocacy Coalition (AVAC) is pleased to announce the release of its annual report examining the state of the AIDS vaccine field. This year's report – *AIDS Vaccines: The Next Frontiers* – warns that a lack of future-oriented planning could slow the pace of AIDS prevention research. *Now* is the time for looking ahead because:

- The next two to five years will bring results from a variety of ongoing trials, including vaccine, microbicide, male circumcision, treatment of herpes simplex virus type 2 to prevent HIV transmission or acquisition, pre-exposure prophylaxis and the female diaphragm as strategies for AIDS prevention. Each new finding means new choices, new messages, new points of convergence and necessary collaboration among trial planners, public health program designers, and communities. The time to begin anticipating and discussing these challenges is now.
- The infusion of new funding that is entering the field means there is an urgent need to map out the pathway for the future: how do we ensure that there is sufficient clinical trial capacity, human resource development and community and political will for the "long haul"? How do we ensure that these the various actors in the field generate new ideas and cross-fertilize each other?
- Finally, the new prevention technology fields can learn valuable lessons from other fields. Recent licensure of Gardasil™, Merck's HPV vaccine, provides the opportunity to explore issues of trial participation, access, delivery and funding. There is no perfect model for the delivery of prevention technologies; there is also no excuse for passing up the chance to collaborate on and learn from rollout of a vital public health tool for cancer protection and sexual and reproductive health.

The report contends that the vaccine field, and the field of prevention research in general, must engage in rigorous debate, dialogue and scenario planning which anticipates the issues that the next few years will bring, and ensures that the wide range of stakeholders are informed and empowered to make decisions to compete against the virus.

AIDS Vaccines: The Next Frontiers is available online at http://www.avac.org/reports.htm. For printed copies of this report, please e-mail avacreport@avac.org.

SIECUS' *Making the Connection* focuses on vaginal practices

The summer 2006 edition of SIECUS's (the Sexual Information and Education Council of the United States) *Making the Connection* newsletter provides several excellent articles about vaginal practices around the world – a topic that is critical to those interested in microbicides, women's health, and HIV/AIDS prevention. The newsletter first provides an overview of harmful traditional vaginal practices worldwide, including douching, hymen repair, virginity testing, female genital mutilation, and vaginal drying. Several articles then go more in depth on:

- Communities working to abandon female genital mutilation
- Genital cosmetic surgery – a high priced new trend in the U.S. and elsewhere
- Vaginal practices in Indonesia including dry sex
- An introduction to microbicides in the context of vaginal practices

Making the Connection is SIECUS' quarterly international newsletter on sexuality, sexual health, and sexuality education. The full issue is available at http://www.siecus.org/inter/connection/conn0059.html

Updated factsheet on Rectal microbicides

Now available on the Global Campaign download centre is an updated version of Factsheet #6 on rectal microbicides. The factsheet is a great accompaniment to either the general microbicides presentation or the more specific rectal microbicides presentation available at the address above. www.global-campaign.org/download.htm

Correction to GC News Issue #69

In GC News #69, we reported on a Microbicides Networking Reception held at the International AIDS Conference in Toronto which allowed microbicide advocates and researchers to reflect on the week's event in an informal setting. We inadvertently omitted Polydex Pharmaceuticals Limited, developers of Ushercell, as one of the event sponsors. Others organizers included the Canadian AIDS Society, the Microbicides Advocacy Group Network, and the MaRS Discovery District.

We welcome your input and contributions for future issues! Please send emails to: info@global-campaign.org.
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