The Global Campaign News
October 10, 2003

Welcome to the biweekly *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 STDs.

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Update from India: National Policy Meeting on Microbicides

On September 29 and 30, the Global Campaign for Microbicides, PATH India, and the Indian Council of Medical Research (ICMR) held a National Policy Meeting on Microbicides and HIV Prevention Options for Women in New Delhi, India. This meeting was in response to a recommendation that emerged from the Community Stakeholders' Meeting on Female Condom and Microbicides held in 2002 in New Delhi. This year's meeting brought together representatives of government, donors, researchers, NGOs, international agencies, medical providers and pharmaceutical industry to discuss policy implications of microbicides research and development, and to consider the complementary activities that leaders can take on to speed access and use of a safe, effective microbicide in India.

Data presented at the meeting demonstrated that while condom use may be increasing among men with casual sex partners, condom use in primary partnerships is extremely low. Meanwhile, 90% of positive women in one study were married, monogamous women who had contracted HIV from their husband. Qualitative data collected from around the country, demonstrated people's interest in microbicides and other women-initiated prevention methods.

In addition to the need and demand for microbicides, India has a rich research portfolio, ranging from screening new compounds for anti-HIV activity and developing animal models for testing products, to investigating approaches to formulation and hosting four different microbicides trials. India also has a well-established drug regulatory body and a strong pharmaceutical industry, opening up the possibility for local initiatives in licensing, manufacturing and distributing proven microbicides.

The meeting addressed the challenges of "partial efficacy," recognizing the challenges of adding a less-than-perfect prevention method to existing strategies. Emphasis was placed on creating strategic messages, doing good behavioral research, and discussing microbicides within the range of prevention tools. Dr. P.L. Joshi of the National AIDS Control Organization (NACO) reiterated the need to continue vigorous interventions on all fronts, including behavior change communication and male and female

condom promotion. Dr. S. Mokkapati of ICMR described the potential of cervical barriers as women-initiated dual protection methods, and planned studies to determine their effectiveness. Dr. Vimla Nadkarni of the Tata Institute for Social Sciences and Dr. Lalita Kumarmagalam from the NGO Prakriti both emphasized the gendered nature of the issue and the need to look holistically at microbicides in the context of sexual and social dynamics between women and men in Indian society. Other issues taken up in the meeting included: determining the public health impact of microbicides, male involvement in microbicide programs, resource and access issues, and the role of communities in implementing appropriate and ethical research.

The meeting resulted with several recommendations, particularly the formation of a multi-sectoral working group on the issue of microbicides, that will include members from the many different interests represented at the meeting. Initial coordination of the group will be taken forward by the Global Campaign and PATH in the coming months. A report from the meeting will be forthcoming and will be posted at www.global-campaign.org

Meanwhile, the Global Campaign is deeply appreciative of the collaboration of our colleagues and partners in this meeting who are too numerous to name but include Mr. Vinay Kumar and Mr. Vivek Srivastava of PATH India and Dr. Ganguly and Dr. Walia of ICMR, as well as old friends Bobby Ramakant, Radium Bhattacharya, and Renu Seth. We are also grateful to USAID for the financial support for this project.

Vaginal ring study may prove appropriate for some microbicides

As reported in the July 23 issue of GC news, researchers at Queen's University in Belfast, Ireland have been working on developing a slow-releasing silicone ring to deliver medications in the vagina over a period of several weeks or months. On Sept. 19, Karl Malcolm and his colleagues presented laboratory findings at the British Pharmaceutical Conference demonstrating that their ring (designed to be worn high in the vagina) could deliver metronidazole, an antibiotic, for 14 days at a sufficiently steady dose to kill Gardnerella vaginalis, an organism that causes bacterial vaginosis (BV).

This is exciting news, even at first glance, because, as Malcolm told BBC reporters, "bacterial vaginosis, and other sexually transmitted diseases, have been widely implicated in an increased risk of sexually transmitted HIV infection." HIV, he noted, "thrives at the elevated pH associated with bacterial vaginosis infection." At present, metronidazole is given orally or in vaginal gel form to treat BV. Oral administration, however, sometimes causes side effects including nausea and vomiting. A more acceptable, user-friendly method of taking the drug could result in decreased prevalence of BV and consequent reduction in HIV risk.

The timing of this research is exciting because it coincides with progress in the development of some "small molecule" candidate microbicides that could be appropriate to load into a vaginal ring. Some of the candidate microbicides now in advanced trials (such as Carraguard and Dextrin Sulfate) have "large, sticky molecules" – making them potentially effective barriers against HIV when inserted in gel form but also rendering them too large to diffuse through the ring's silicone membrane. Some "second generation" microbicides, however, have smaller molecular size that may make them suitable for loading into a vaginal ring. One such candidate, UC-781, is now about to enter human trials.

Biosyn (the Philadelphia-based developers of Savvy) announced last month that their new candidate product, UC-781, would be entering a Phase I safety trial in Norfolk, VA. Funded by CONRAD (the Contraceptive Research and Development Program), this trial will enroll 48 women and will test three different strengths (0.1%, 0.25% and 1.0%) of UC-781 gel, comparing its impact on vaginal tissue to the impact of a placebo gel. UC-781 works as a reverse transcriptase inhibitor; a drug designed to prevent HIV from replicating itself effectively.

HIV infects by hi-jacking healthy cells and overwriting their DNA with its own genetic code. This re-programs the cell and forces it to create more HIV when it reproduces, instead of more healthy cells. HIV, however, carries genetic material in the form of RNA, rather than DNA. The fact that HIV relies on RNA, rather than DNA, is part of what enables it to mutate so freely in response to the drugs used to treat it and to generate drug-resistant mutation strains with such rapidity.

Using an enzyme called reverse transcriptase, HIV converts its RNA into DNA -- thus enabling it to overwrite the healthy cell's DNA. Reverse transcriptase inhibitor drugs inhibit HIV's ability to use its reverse transcriptase enzyme to do this conversion, thus preventing the virus from hi-jacking healthy cells. Several different types of reverse transcriptase drugs have been developed to date and are being used in various combinations by many people living with HIV. All of them, however, use some mechanism of action that blocks HIV's use of the reverse transcriptase enzyme.

According to Biosyn, UC-781 has also demonstrated a "memory effect" in vitro. Cells treated with UC-781 in a test tube seem to be protected against HIV infection for several days. This memory effect, if borne out in human use, could further contribute to UC-781's microbicidal effectiveness. A strong, public demand exists for a microbicide that could be applied several hours before intercourse. The intersection between the vaginal ring research and the UC-781 research described above conjures up the dream of an HIV-specific microbicide with memory effect that could be loaded into a slow-releasing silicone ring and remain active in the body for weeks at a time.

Unfortunately, this scenario is still several years away at best. Nevertheless, the very possibility of it illustrates the spirit of synergy and inventiveness that is now possible in the field of microbicide development. And dreams, however far-fetched, are the very fuel of invention.

Many thanks to AIDSMed.com and thebody.com for assistance in describing the function of reverse transcriptase inhibitors.

New coordinator in Europe to expand microbicide advocacy

The Global Campaign is pleased to announce the hiring of Rebekah Webb (rwebb@global-campaign.org) to serve as the coordinator of Global Campaign Europe, a joint initiative of the GGM and our partner group, International Family Health(IFH), in London. Rebekah joins us from her previous position at the National AIDS Trust, a policy and advocacy organization in London, where she worked on vaccine and microbicide policy and helped coordinate the UK-Ireland Campaign for Microbicides – our first GC Europe node.

Based in Brussels, Rebekah will help expand and coordinate Campaign activities in Europe over the next two years. She will be identifying and supporting new partner groups, defining critical policy questions, and rolling out a media strategy. We hope to see at least four more European nodes established in by the end of 2004. Each of these advocacy groups (like those in North America) will work on making microbicide research and access a priority within its own national research. Rebekah will also be working with the European advocates collectively and other European partners, including the International Partnership for Microbicides (IPM) and IAVI, to design and implement strategies for mobilizing support for microbicides within the European Union's government as a whole.

Advocates Host Meeting on Microbicides for Nordic NGOs

On September 11-12 in Copenhagen, the AIDS-Fondet, a GCM/IFH partner group sponsored a successful meeting to raise awareness and generate action on microbicides among Nordic NGOs. Representatives

from 15 Danish, Swedish and Norwegian organizations attended the meeting, most from HIV/AIDS-focused NGOs but some representing family planning and international development agencies.

The meeting featured presentations by (among others) Zeda Rosenberg of IPM, Rebekah Webb, and Yvonne MacPherson of IFH. Other speakers included Henriette Laursen, AIDS Fondet (Denmark) and Peter van Rooijen, AIDS Fonds (Netherlands).

The Copenhagen meeting concluded with a discussion of what participants needed in order to take advocacy and mobilization efforts forward in their own countries. Rebekah will be working with them on implementing the action steps they identified, translating Global Campaign materials into the appropriate languages and discussing potential organizing strategies that could work in Scandanavia. A second organizing trip in planned for November, at which time we hope to formally establish the first Scandanavian Global Campaign node.

Some developments look promising for rectal microbicides

In 1997, Michael Boyd and colleagues at the National Cancer Institute announced that they had isolated an antiviral protein called cyanovirin-N (CV-N), that appeared during in vitro testing to have anti-HIV properties (Boyd MR, Gustafson KR, et al. in *Antimicrobial Agents and Chemotherapy,* v. 41 n. 7, pp. 1521-30). Derived from a blue-green algae called cyanobacterium, CV-N binds to the sugars attached to HIV envelope protein and prevents them from binding to mucosal cell surfaces in the vagina or rectum. CV-N also appeared in vitro to have some activity against HSV-2 (herpes).

Last July, Che-Chung Tsai and colleagues at the University of Washington presented evidence that Cyanovirin-N was capable of preventing rectal transmission of SHIV (simian immunodeficiency virus) transmission in macaques (Tsai Che-Chung; Emau Peter; et al. in AIDS Res Hum Retroviruses 2003 Jul; 19 (7): 535-41). In their studies, none of the macaques treated with either the 1% or 2% CV-N gel showed evidence of SIV infection and neither CV-N nor placebo gels produced any adverse effects in any macaque following the rectal application.

These study results and others underway on CV-N strongly suggest that it warrants expanded investigation as a potential microbicide to prevent HIV transmission in humans. Work is also underway to develop new technologies for effective delivery of a CV-N microbicide. Investigator Gianni Pozzi, of the University of Siena, told Reuters Health last August about his efforts to “engineer commensal bacteria to produce a potent HIV-specific microbicide such as cyanovirin." These bacteria, if genetically engineered to colonize the vagina and release the microbicide, may be able to deliver a protective effect that is long-lasting and does now affect the vaginal ecosystem. Dr. Pozzi’s findings to date appear in July 5th issue of *AIDS (*AIDS 2002; 16:1351-1356).

Biosyn, the Philadelphia-based developer of two other candidate microbicides (Savvy and UC-781) is now pursuing the preclinical development of CV-N as a potential microbicide and is planning additional macaque SHIV studies to determine the minimum effective dose for the prevention of HIV transmission. Given the paucity of rectal microbicide research currently underway, we hope that the advent of CV-N will spur increased interest among developers in pursuing rectal as well as vaginal microbicide development. With at least one product in the pipeline showing demonstrable potential for preventing rectal transmission, now is the time to expand this vital line of inquiry and move toward meeting the needs of gay men and the many women who also engage in anal intercourse.

We welcome your input and contributions. Correspondence can be addressed 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