



## Global Campaign Research Update 16 January 2008

### *Research update*

#### Update on follow-up to Cellulose Sulfate trial closure Global

As most GC News readers will be aware, in late January 2007, the data safety monitoring boards for two trials of the candidate microbicide Cellulose Sulfate (CS) made the decision to close the phase 3 clinical trials. Given that almost a year has past, GCM felt that it was important to check back with trial staff to follow up on the close-out of the CS trials. For more information about the CS trials, visit: <http://www.global-campaign.org/CS.htm>

Right before the holidays, GCM sent a series of questions to Lut Van Damme, currently Senior Scientist at Family Health International (FHI), and formerly the principal investigator (PI) of the CS trial for CONRAD, and Vera Halpern, principal investigator of the CS trial for FHI. Below we reproduce our correspondence.

#### *Question 1 from GCM: What follow-up activities were or are being conducted with trial participants?*

**CONRAD:** The gels were immediately collected from the participants after halt of the trial and the results were immediately communicated to individual participants and community members. Several months later after the final analysis was done, the investigators talked again to local IRBs [international review boards], regulatory agencies and participants before results were made public at the International AIDS Society (IAS) Conference in Sydney. Follow up visits with the participants were conducted and completed by 31 March 2007. Besides trial participants, we also immediately (at trial halt) informed all regulatory bodies (FDA and local regulatory agencies in the trial countries through the investigators) and all ethical/institutional review boards.

**FHI:** All participants were contacted via phone immediately after it was announced that the study was closed and told to stop using the gel and return to the clinic for the final appointment. During the final appointment all unused gels were collected and all participants were tested for HIV and STI as usual. It was explained that we closed our trial because of the safety concerns raised in the parallel CS study even though there was no apparent increased risk of HIV among CS users in the Nigerian trial.

#### *Question 2 from GCM: What percent of trial participants have been contacted by staff?*

**CONRAD:** The staff reached out to all of the participants but 10% were lost to follow up.

**FHI:** Site staff made an attempt to contact all participants via telephone; at least three contact attempts were made for all participants. Special efforts were made to bring back the participants who were in active follow-up at the time of the study closure (i.e., not lost to follow-up.)

#### *Question 3 from GCM: Advocates would be very interested to hear about participants' reactions, questions, etc. Of course specific conversations are confidential, but any general thoughts would be interesting.*

**CONRAD:** In some sites we had to provide a lubricant gel in exchange for return of the study gel because women very much appreciated the lubricating quality of the gel. I heard of only few women who were truly upset in Durban because of the media coverage in the City Press which portrayed the women as guinea pigs, and uneducated. Investigators reported that many women were disappointed the trial stopped.

**FHI:** The common reaction was: "Why do you close our trial in Nigeria if the gel didn't work in South Africa?" The participants tried to stock gel towards the final visit and were reluctant to return unused supplies even after they

knew the reason for the early closure. The majority found gel “very pleasant” and conveyed that it enhanced their sexual experience.

***Question 4 from GCM: What analyses of the data have been completed, are underway, or are planned?***

**CONRAD:** Intent to Treat analysis (includes all women who were randomized and for whom there is an HIV follow-up result) and per protocol, which stops women’s contribution at the time when they are taken off product (e.g. because of being pregnant). We looked at HIV, STI, sexual behavior and gel use data, adverse events etc. More exploratory analyses are being done.

**FHI:** Primary analyses of HIV, STI, pregnancy and acceptability data have been completed. Secondary analyses are underway. We have plans for a number of additional analyses and papers (e.g., performance of the HIV testing algorithm; predictors of HIV and pregnancy).

***Question 5 from GCM: Are there any lessons learned from this process that you would share (publicly) for future trial closures?***

**CONRAD:** Good support in dealing with the media is essential and in general, I’m pleased with how it was reported. Collaboration, early communication within the microbicide community and task sharing are essential. With our own experience and the current stories about the Phambili trial, we realize how hard it is to inform the South African press in a way that a story is accurately reported.

**FHI:** Research on possible methods of HIV prevention can only be done with the involvement of people who volunteer to participate in trials, communities hardest hit by HIV/AIDS, health officials, civil society groups and scientists dedicated to public health. These partnerships are essential to the research endeavor. We’re pleased to see how such partnerships are evolving. In general, each trial builds greater understanding among HIV stakeholders of how best to collaborate, and each trial brings us closer to finding ways to prevent HIV transmission.

***Question 6 from GCM: Is there anything else that you think would be useful to share with advocates?***

**CONRAD:** We want advocates to know how much we appreciate their help in getting correct information to people. If advocates have concerns/doubts or criticisms, we ask that you bring these concerns or questions to us directly first, rather than to raise questions in the media that could fuel rumors.

**FHI:** Both principal investigators in Nigeria are having dissemination meetings with the local advocates, communities, researchers and other HIV stakeholders on state and national levels.

***Question 7 from GCM: What has been done to ensure access to treatment for those who seroconverted? And how is the money that was set aside being managed in order to ensure that this happens? We understand that this was the trial site’s responsibility, and we can contact the sites directly for a separate follow up article if you aren’t able to answer this question.***

**CONRAD:** CONRAD asked written agreements between the study team and the referral sites. Special funding was set aside for the care of seroconvertors for 5 years. Special contracts in this regard were made with each site where there were seroconvertors. CONRAD transferred the money to the appropriate study teams who deal with it further.

**FHI:** According to the CS Phase III protocol all participants who were diagnosed with HIV, either at the screening or during the study, received HIV post-test counseling from trained personnel in the study clinic. Participants were also encouraged to return to the clinic at any time to discuss any concerns or questions they might have.

In addition, all HIV positive participants received a referral letter signed by the Principal Investigator or sub-investigator to attend one of the several designated HIV care and treatment centers. They were also given a complete list of providers that offered HIV services with the cost of the services (if any) and the physical address and telephone numbers of the referral centers. Referral procedures and provision of HIV treatment differed slightly between the two sites:

*In Lagos:* The PI had written and verbal agreements in place with three treatment centers and two NGOs that provided counseling and support to people living with HIV. All treatment centers in Lagos are part of the PEPFAR program; they do not charge for admission and provide free treatment.

*In Port Harcourt:* The PI had verbal agreements in place with two treatment centers and one center that provided counseling and support to people living with HIV. The PEPFAR program was not active in the Delta region of Nigeria at the time of the trial. Both treatment centers in Port Harcourt were subsidized by the local government and by the Global Fund. They both had a baseline assessment fee but subsequent HIV treatment was provided for free. In order to address the problem of this fee in Port Harcourt, the CS study allocated a certain percentage of the budget to cover this expense for all study seroconverters as well as the women diagnosed with HIV at screening. In addition, one of the PEPFAR centers in Lagos agreed to accept the study participants from Port Harcourt if they were willing to relocate.

In general, very few study seroconverters sought HIV counseling and treatment during the study. We re-contacted all HIV-positive participants that previously might have refused to attend HIV treatment centers in order to inform them of the study closure and encouraged them to enroll into the existing reliable and sustainable HIV treatment programs subsidized by the PEPFAR program in Lagos or by the local government in Port Harcourt before the study was closed. In addition, all participants, including seroconverters, were provided with phone numbers of the site PIs, study coordinators and outreach workers and encouraged to contact them directly after the end of the study in case of any study-related problems or questions. The PI in Port Harcourt will contact FHI with any HIV treatment-related questions so FHI can consider additional provision of funds to cover the admission fee on a case by case basis.

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