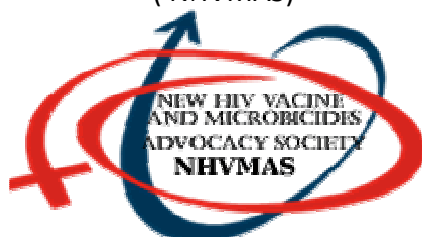

Oral Tenofovir Controversy II: Voices from the Field

**A series of reports of the Oral Tenofovir Trials from
the perspectives of Active Community Voices engaged
on the field in Cambodia, Cameroon, Nigeria, Thailand
and Malawi**

A project of the
New HIV Vaccines and Microbicides Advocacy Society
(NHVMAS)



with support from **SIDACTION**

Compiled by Morenike Ukpong and Kris Peterson

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About NHVMAS

NHVMAS (pronounced 'navmas') is an acronym for the **New HIV/AIDS Vaccine and Microbicide Advocacy Society**. It is a civil society group – committed to mobilizing popular participation and public support for the new HIV prevention technology research and development in Nigeria. Its mission is to accelerate HIV/AIDS policy implementation and ensure accountability in the context of new HIV/AIDS prevention tools development in Nigeria.

Its vision is to see to the halt of the spread of HIV/AIDS in Nigeria by ensuring the availability of safe, effective, acceptable, affordable and locally relevant HIV prevention tools for all Nigerians as soon as they are available. The group advocates on all issues that would ensure the realization of its vision as well as monitors all HIV research activities to ensure that the rights of all heroic volunteers are safeguarded.

NHVMAS is open to all Nigerians and seeks to partner with as many groups as possible.

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Preface

Research is currently taking place in a manner that could change the way we think about preventing HIV infection. The researches described in this report have already changed the way we think about research. Over the past six years, multiple clinical trials have been designed and implemented in Africa, Asia, and the Americas to test Tenofovir – an existing antiretroviral drug that is now widely used in treatment of HIV and AIDS – alone or in combination, for possible use as a product that HIV-negative people could take regularly to reduce their risk of HIV infection.

This potential application of Tenofovir or Tenofovir plus emtricitabine is called pre-exposure prophylaxis, or PrEP. With five million new HIV infections every year – almost 600 every hour – a biomedical tool to prevent HIV could have a profound effect on our ability to control the AIDS pandemic.

We truly need as many HIV prevention tools as possible. Research on PrEP, vaccines, microbicides and other potential interventions are important for HIV prevention. Yet PrEP research – especially the early trials in Africa that are documented in this report – have not been easy or without controversy. At different points in the history of the researches described in this report, there were assertions that the studies were unethical on several counts, including inadequate provision of HIV prevention counseling for volunteers, lack of treatment for HIV infection acquired during the trial, an insufficient informed consent process, and limited involvement of communities in trial design.

These were real concerns that demanded immediate attention, and yet thorough and unbiased investigations and reports of each situation were slow to develop, leaving the field mired in accusations, delays and missed opportunities.

As this important report from NHVMAS articulates, the primary lesson of these controversies is that communities must be meaningfully, productively engaged in research.

Research must be done with (not on) communities. Scientists, communities, advocates, policy makers, funders, sponsors, regulatory bodies and the media have a responsibility to work together to improve and expedite the process of finding new prevention and treatment options.

The concerns raised throughout the narrated history are solvable; and they must be solved so that the real concern – the need to develop additional HIV prevention tools – can be properly addressed. This important historical record is a clarion call to researchers, advocates and policy makers that any perceived problems and concerns with research must be identified, solutions developed in partnership with local communities, and then the trials should continue.

PrEP research is important. NHVMAS – and especially the voices from the field that call out in this report – once again remind us that HIV prevention research is not easy, but it is vital.

Mitchell Warren,
Executive Director, AIDS Vaccine Advocacy Coalition (AVAC)



Introduction

Prior to 2004, there had been some concerted efforts in the field of HIV biomedical clinical research to encourage active community engagement in the development and implementation of clinical research. Advocates of community engagement were keen to ensure that communities had a voice in designing the research that was of critical interest to them, whether that research was about testing new treatments for HIV positive individuals or whether it was about developing products that could prevent HIV infection.

Interestingly, the demand by community advocates for the right to participate in decision-making in prevention trials were stronger than those demands for community engagement in trials designed to test a new treatment regimen. In 2004, these demands reached a crescendo when communities in which phase IIB PreP – prevention of HIV infection prior to exposure using antiretrovirals orally – clinical trials were being conducted organised themselves to ask questions and demand answers about the trial they were being asked to participate in.

This report documents community advocates' perspectives of the events around the oral pre-exposure prophylaxis tenofovir controversy that took place in five countries between 2004 and 2006. These are anecdotal accounts that try to capture, as accurately as possible, the events that unfolded and transpired from within their respective communities.

The names of stakeholders involved in these reported controversies, and those who may otherwise be considered as actively involved in the evolution of events, were not included in this report. This is because the authors could not contact these actors for possible corroboration of the information provided by the community advocates who gave the anecdotal accounts in this book.

The authors of this document worked with the authors of each piece to ensure accuracy of the report as much as possible. Queries were raised and responses from narrators were explored beforehand.

The Cambodia piece is an abridged version of an extensive investigative report by its authors. The Cameroon report is an abridged version of an interview conducted with Calice Talom Yomgne by one of the authors.

The analysis in the final chapter was based on inferences drawn from the reports on the controversy.

This report focuses on the experiences and perspectives of community members with intimate knowledge of the trials and, indeed, the report is intended to provide a space for their experiences to be respectfully shared and considered.

As a result of our decision to highlight community-based narratives, the perspectives of other actors/stakeholders involved with the trial have not been included here.

Chapter 1:

The Cambodia Story¹ :

Anna Forbes², Sanushka Mudaliar³

In 2004, researchers from the University of California San Francisco and the University of New South Wales, together with the Cambodian Ministry of Health National Centre for HIV/AIDS, Dermatology and STDs (NCHADS), prepared to launch a clinical trial in Phnom Penh. The trial was to determine whether a drug called *Tenofovir disproxil fumarate* (TDF) was safe and effective for use as a pre-exposure chemoprophylaxis to prevent HIV transmission. In August 2004, before the trial formally began, preparations for it were halted by the Cambodian Government following protests led by Womyn's Network for Unity (WNU), the Union of Cambodian sex workers.

This report reviews the events leading up to the cancellation of the trial. It is based both on interviews conducted in Cambodia and telephone interviews, with those key players who were available for interview. The interviews were conducted over a two-year period between mid-2006 and mid-2008. There is no single version of events that constitutes the "real story" of the Cambodia Tenofovir trial. The researchers, NGO staff, and WNU members interviewed presented different and sometimes incompatible accounts of the events surrounding the trial.

Given this reality, we have focused on capturing as accurately as possible the political context and backdrop against which these events occurred. We hope that this report sheds new light on a controversial episode in the history of HIV prevention research and, thus, enables us to learn from it.

Background – The Political Climate for Cambodian Sex Workers in 2004

Prior to 2000, various NGOs in Phnom Penh offered programs for sex workers. Seven of the main NGOs working in this area joined forces in 2000 to support their sex worker groups' decision to create an independent union led and controlled by members of the sex worker community. This major step forward fostered greater sex worker autonomy, helped to build

¹ This is a summary of a paper entitled, "Preventing Prevention Trial Failures: A Case Study and Lessons for Future Trials from the 2004 Tenofovir Trial in Cambodia" by Anna Forbes and Sanushka Mudaliar, published by the Global Campaign for Microbicides (2009).

² An accomplished organizer, writer and advocate, Anna Forbes has worked in HIV/AIDS since 1985 and in women's health and human rights since 1977. She is now the Deputy Director for the Global Campaign for Microbicides. She serves as GCM's liaison with the international Network of Sex Work Projects, the International Community of Women Living with HIV/AIDS, among other global and national advocacy coalitions and collaborations. Anna's writing has appeared in the popular press, peer-reviewed journals, professional anthologies, and a series of children's books she wrote on HIV/AIDS.

³ Sanushka Mudaliar works with the Association for Women's Rights in Development (AWID). This paper was written in her personal capacity. She has previously worked on research and campaigning with young women in the Cambodian garment and sex industries, and on youth-led social justice initiatives with the International Youth Parliament

their capacity to implement their own community programs, and encouraged sex workers to articulate their rights and needs. Thus, the Womyn's Network for Unity (WNU) was born.

This increased attention to the role of sex workers in HIV prevention was due, in large part, to Cambodia's 1998 adoption of a 100% Condom Use Program (CUP) that mandated condoms as part of every commercial sexual encounter. According to Population Action International, consistent condom use more than doubled among brothel-based sex workers in Cambodia between 1997 and 2001 and their HIV infection rates declined⁴.

Amongst other things, the 100% CUP policy required sex workers to carry government identification cards documenting their regular check-ups for sexually transmitted infections. This had the effect of making it easier for the police to locate them, extort money from them, and abuse them—practices that were well-established before the 100% CUP and further facilitated by its implementation.

The political climate took another sharp downward turn for sex workers in May 2003 when the US Congress passed the Global AIDS Act to allocate \$US15 billion over five years through an initiative known as the President's Emergency Plan for AIDS Relief (PEPFAR). While PEPFAR was a step forward in terms of overall investment in HIV/AIDS work, the Act contains an insidious provision that became known as the Prostitution Pledge.⁵ The Act states that "No funds . . . may be used to provide assistance to any group or organization that does not have a *policy explicitly opposing* prostitution and sex trafficking."⁶ (emphasis added) All grantees are also required to refrain from activities that could be construed as condoning sex work in any way, even if the grantee pays for those activities with other funds.

Not surprisingly, the Prostitution Pledge had an immediate impact on the sex worker community, the organizations engaging with them, and all subsequent attempts to cultivate dialogue with sex workers – including those made by trial staff. All of the NGOs running sex worker programs in Phnom Penh in 2003 received USAID funding. Womyn's Agenda for Change, one of the seven NGOs that supported the creation of the WNU, chose not to sign the pledge and to continue to support the WNU with technical assistance. The other six NGOs signed the pledge and withdrew from their involvement with the WNU.

It was in the context of this environment that the trial team began consulting with local NGOs and asking for their help in recruiting trial participants. The ambient political upheaval caused confusion in two directions. Some of the NGO staff interviewed for this paper, for example,

⁴ Population Action International. Cambodia and HIV: Winning Round Two in a Preventive Fight, Research Commentary, volume 1,

⁵ Franck Masenior N and Beyrer C. The US anti-prostitution pledge: First amendment challenges and public health priorities. *PLoS Medicine* PLoS Medicine Vol. 4, No. 7, e207 doi:10.1371/journal.pmed.0040207

⁶ *United States Leadership against HIV/AIDS, Tuberculosis, and Malaria Act of 2003*, 22 U.S.C. § 7631(f) (2003) [commonly referred to as the Global AIDS Act].

wrongly believed that the US-based PrEP trial researchers were connected to USAID and that the level of support they showed for the trial would directly affect their future USAID funding.

The same presumed association between the researchers and USAID made some sex workers extremely suspicious of the motivations of the research team.

Chain of Events

Cambodia had virtually no experience with clinical trials among highly vulnerable populations prior to the planning of the PrEP trial⁷. In 2003, the Cambodian Ministry of Health convened a National Ethics Committee to review the trial protocol. A preliminary protocol was submitted to the Cambodian Ethical Review Board and subsequently approved. The draft protocol for the Cambodia PrEP trial included the following provisions:

- Participants would receive \$US3 per month compensation for their participation in the trial for 12 months. (The monthly income of a rural female sex worker was documented in 2003 as \$US14.5)⁸
- All volunteers would be screened for HIV in order to identify negative women eligible to enroll in the trial. Positive women who were identified during the trial screening process would be referred to the NCHADS HIV Clinic but would not receive preferential access to the clinic services or other services from the trial
- During the trial, participants were to receive counseling about risky behaviour, free condoms, and free screening and treatment of STIs
- Each participant was to receive an HIV test monthly. Participants who seroconverted during the trial would be given preferential access to free, comprehensive care and treatment at the NCHADS Clinic including access to anti-retroviral therapy if medically indicated, in accordance with Cambodia's national treatment guidelines
- Participants would receive treatment for side effects during the trial, but aside from the HIV care noted above, no treatment would be available for side effects or illnesses developed after the trial had finished

⁷ John Kaldor, personal e-mail communication, 22 September, 2008.

⁸ H Sopheab, P M Gorbach, S Gloyd and H B Leng, Rural sex work in Cambodia: work characteristics, risk behaviours, HIV, and syphilis. *Sex Transmitted Infections* 2003;**79**:e2. available online at <http://sti.bmj.com/cgi/content/abstract/79/4/e2>

Informing the Community and Other Stakeholders: In early 2003, draft information about the trial was distributed to stakeholders including all NGOs with sex worker programs. Discussions with relevant individuals were initiated about the proposed participant recruitment strategy. In late 2003 and early 2004, the research team began holding focus groups as well as larger consultative fora to introduce and discuss the trial with sex workers, NGOs and other members of the community.

As part of the consultation process, the research team contacted local NGOs that engaged with sex workers in Phnom Penh, inviting them to attend meetings about the trial and relay the information they received from the trial staff to the women with whom they worked. Some of the meetings were conducted in English, with translators available as needed, while others were conducted in Khmer.

One NGO worker present at these meetings observed that some sex workers also were invited to participate in these community meetings, “but they generally didn’t speak up very much”.⁹ She attributed this to the climate of intense distrust between many of the sex workers and the NGOs that had developed in the aftermath of the anti-prostitution pledge. Class, gender, and language differences also may have contributed to this reluctance. Some participants reported other factors that prevented the meetings from being as productive as hoped. These included:

- Lack of research literacy: most participants needed basic, easily accessible information about clinical trials and how they are conducted. Without this, participants had no real context for the information they were receiving
- Meetings were described as long and tended to cover the same issues with very little forward motion or change. Several participant concerns were raised repeatedly, especially by the WNU, but never really addressed and questions often went unanswered. This created the impression that the conveners had no real intention of modifying or adjusting the trial protocol in response to concerns and feedback received
- The trial staff was generally represented by researchers from the US and Australia and one Cambodian government official who said very little
- WNU leadership tended to be vocal at the meetings. Other Cambodian and international NGOs working with sex workers were also invited but some of these were simultaneously trying to engage sex workers in the trial while backing away from them in other contexts to meet the anti-prostitution pledge. This dissonance was inevitably counterproductive.

⁹ Interview with Supriya Pillai, 31 January 2006.

The primary concerns raised by participants at the meetings included:

1. How would informed consent be assured?
2. Why and how was Cambodia selected for this trial? Why hadn't they (the participating NGOs and sex workers) been asked if they wanted this trial to occur in their community?
3. How would future access to care, especially ARVs, be assured to seroconverters?
4. What would happen when a trial participant fell pregnant during the trial and/or experienced drug side effects?
5. Would treatment and care be made available to trial participants who experienced drug side effects in both the short and long term after the trial had closed?

A 13-member Community Advisory Group (CAG) was constituted with a mix of representatives of local health NGOs, NGOs serving sex workers, multilateral and bilateral agencies, government health agencies and one unaffiliated sex worker. It met in March and May of 2004.

The CAG process was new to both the researchers and most of the members. The researchers viewed it as a mechanism to raise and resolve a range of issues related to the trial. Several CAG members, however, reported feeling as though the researchers interpreted their questions and suggestions as indications that the speaker simply did not understand the issue raised. They responded by re-explaining the issue rather than by initiating discussion to explore the speaker's concern and consider how it might best be addressed.

NCHADS also formed an external advisory board for the trial which "brought together key governmental departments and international organisations with an interest in HIV and AIDS, including UNAIDS (Joint UN Programme on HIV/AIDS) and WHO.¹⁰" The board met in January and June 2004.

Women's Network for Unity responds to the Trial: Womyn's Agenda for Change (WAC- a technical support organization of the WNU) was among the stakeholders contacted with preliminary information about the proposed trial in early 2003. Members of the research team also met with Rosanna Barbero, the then-director of WAC, and she recalls thinking then that WAC needed to learn more about the potential benefits and risks associated with clinical trials, in case the WNU was asked to become involved in the trial¹¹. Two interns from the University of Michigan Law school were working at WAC at the time and Barbero asked them to do some research on clinical trials, including finding relevant case studies. Barbero and other WAC staff worked with the interns to compile information, particularly regarding the experiences of

¹⁰ Page-Shafer K, Vonthanak S, Penh Sun L, et al. HIV prevention research in a resource-limited setting the experience of planning a trial in Cambodia. *The Lancet*. 2005; 366: 1499-1503.

¹¹ Telephone communication with Rosanna Barbero, 5 December, 2008.

participants in past clinical trials so that, if asked, they could provide a balanced picture of what potential participants might expect if recruitment for the PrEP trial started in Cambodia.

Several months later, WAC received an invitation to attend one of the information sessions at NCHADS about the trial. Their sex worker program coordinator, Phoung Phally Pry, invited members of the WNU to accompany her to the meeting. Several members of the WNU also attended focus group discussions around this time and the trial quickly became a hot topic of discussion at WNU meetings.

The WNU secretariat asked for WAC's assistance in providing additional information to answer their members' questions about both the positive and negative aspects of potential trial involvement. WAC agreed to provide the information it had collected and saw this support as one more step in empowering the WNU to define its own position regarding the trial. It is important to recall that WAC had been providing this kind of technical assistance and capacity-building support to WNU since the union's inception; a vital function given that none of the WNU Secretariat read English. The ideological basis of both organizations is such, however, that WAC fully appreciated WNU's autonomy and did its best to serve as an objective transmitter when meeting such information requests.

The WAC staff and interns relayed their findings on clinical trials in a workshop for WNU members in early 2004. After the workshop, the WNU convened a membership meeting to discuss the new information and formulate their response. The members expressed particular concern about the risk of Tenofovir side effects, noting that the trial materials cited bone density loss and kidney failure as possible serious side effects. It was at this meeting that sex workers, themselves, came up with the idea of asking for insurance.

At that time, no studies had been published on the possible safety consequences of on-going tenofovir use among HIV negative people¹², so no real data existed with which to answer these concerns. Members were particularly concerned about their economic, as well as physical well-being. For many, their work provided the sole source of income for their children and other family members. Any side-effects that rendered them unable to work (even briefly) could result in hunger and instability. Participation in the trial, therefore, could pose real and immediate risks to individuals and their families.

The members decided it was reasonable to ask that the risk taken by participants' be offset by some kind of long-term insurance protection.¹³ They decided to ask for health insurance for 20-30 years to cover medical expenses generated by the possible side effects of Tenofovir (not general insurance for all medical problems, as has been mis-reported by some media sources). They also decided that \$US3 per month was insufficient compensation for their involvement,

¹² Melanie Thompson. *AIDS Patient Care and STDs*. January 1, 2005, 19(1): 1-4.

¹³ Group interview WNU members, 23 June 2006.

since even the minor side effects listed in the trial materials, such as stomach or headaches, could reduce their ability to work and earn money.

According to the WNU secretariat,¹⁴ members began explicitly asking in trial-convened focus groups and meetings that some kind of long-term insurance be provided to cover the possibility of long-term side effects. The trial staff at these meetings said that they were not empowered to discuss this, but agreed to find the answers and respond. Several stakeholders interviewed concurred that questions went unanswered and that they knew of no transparent mechanism for getting responses to questions that could not be answered at the meetings. The researchers were undertaking efforts “behind the scenes” to provide compensation to participants whose health was seriously affected by trial participation, but this was not clearly communicated.

After having raised these concerns repeatedly in focus groups and meetings, WNU members became frustrated that their questions were not being adequately answered. They viewed the researchers as unwilling to take seriously their concerns about the health of sex workers who were potential trial participants.

The WNU had observed that press conferences convened by other advocacy groups has successfully drawn public attention to concerns that were not being addressed and thought that the technique might work for them, as well. The WNU decided to hold a press conference to bring the discussion to a head in a forum not convened by the research team. The press conference was held on 19 March 2004.¹⁵

The day after the WNU press conference, about 12 WNU members were invited to a focus group conducted in Khmer where they discussed their concerns and issues. The focus group was recorded and the issues documented in English¹⁶. Sotheavy Sou and Sok Chea from the WNU report being told at this meeting that insurance for participants was out of the question, and that if WNU did not let go of the demand for insurance, then they would be bypassed in the recruitment of participants for the trial.¹⁷

At this point, events began to escalate and the chances for a non-confrontational resolution diminished. The WNU responded to the researchers’ declaration by issuing its own ultimatum. They told the press that if the research team failed to provide insurance for participants, then they would boycott the trial. “We will go ahead with it if they give us insurance. If they decline... we will oppose the drug from being brought into Cambodia and being tested on our

¹⁴ Group interview WNU members, 23 June 2006.

¹⁵ Women’s Network for Unity, “Background to WNU Press Conference on Tenofovir Trials in Cambodia on March 29, 2004”. Available on line at <http://wnu.womynsagenda.org/documents/wnu29mar04.pdf>.

¹⁶ Margery Lazarus, personal e-mail communication, 15 September, 2008.

¹⁷ CBS News “AIDS Drug Trial Sparks Static” broadcast on 30 March 2004.

women.”¹⁸ The WNU continued to attend public meetings and discussions about the trial held by the research team or NGOs to present their perspective.

Members of the research team also responded to the press conference by publicly questioning whether WNU actually represented the views of the broader sex worker community. In media reports some trial staff stated that they thought the WNU was not demanding insurance solely on behalf of Cambodian sex workers but were being influenced by WAC or other external groups opposed to medical trials on principle.

Andrew Hunter of the Asia-Pacific Network of Sex Workers summarized the WNU members’ decision to demand insurance as follows: “What the sex workers actually wanted was protection against the possible health consequences of side effects. Insurance was how this was expressed in their campaigning. The researchers refused to accept that Cambodian sex workers had the information, knowledge and personal empowerment to sit down and negotiate as equals. They could not fathom that sex workers could have a representative agency that could speak for them as a group.”¹⁹

The decision by the research team to question the WNU’s legitimacy as representatives of the sex worker community exacerbated the adversarial tone that the debate had taken. The WNU felt it implied that, because the sex workers were relatively uneducated, they could not have identified the concerns they raised on their own, but only with the direction and guidance of outside activists. It also suggests that because WNU chose to access external assistance, they were not capable of acting independently. As discussed above, WNU accesses technical support and assistance as needed from WAC. Because of the USAID Prostitution Pledge”, WAC was the only NGO still working with WNU. Since none of the WNU secretariat reads or speaks English, WAC staff translated trial information and provided translation services for WNU members at meetings. At WNU’s request, WAC also prepared a workshop to brief WNU members. As WAC Director Rosanna Barbero put it, “Sex workers should know their rights. In this situation, when the WNU asked us questions about the trial, we didn’t have answers so we did some research on their behalf.”²⁰ Barbero reflected on the situation with the comment, “Those who hold the view that the WNU’s reaction was masterminded by radical anti-corporate activists can’t possibly have ever spoken to the WNU directly. They fall just short of saying that the sex workers are stupid, illiterate and uneducated and that therefore it must have been western activists who controlled their agenda.”²¹

¹⁸ Associated Press. Workers May Opt Out of Cambodia HIV Study. 26 Mar. 2004. <http://www.heraldsun.com/healthmed/34-463177.html> (4 June 2004)

¹⁹ Interview with Andrew Hunter, 28 June 2006.

²⁰ Interview with Rosanna Barbero, 21 June 2006.

²¹ Interview with Rosanna Barbero, 21 June 2006.

Some members of the WNU attended the 2004 International AIDS Conference held from 11-16 June in Bangkok. At the Conference, they were introduced for the first time to ACT UP/Paris. With the support of ACT UP/Paris and members of other sex worker advocacy organizations, the WNU staged a highly visible protest on June 14 against Gilead (the manufacturer of Tenofovir) during a Gilead-sponsored satellite session on ARVs.

The 14 June protest at the International AIDS Conference in Bangkok resulted in a firestorm of media attention. On 15 June, the WNU held another press conference reiterating the demand for insurance and calling for the trial preparation process to be “better and more honest, with sex workers not pressured or given wrong information about the drug.”²² The WNU also wrote a letter to the Cambodian Prime Minister Hun Sen outlining its concerns about the trial. No response to this letter was received.

Trial Preparation Stops: On 3 August, 2004, at the groundbreaking ceremony for a new hospital, Prime Minister Hun Sen made the following statement: “Cambodia is not a trash bin country...they should not conduct experiments with Cambodians. They should do it with animals.”^{23, 24, 25}

In Cambodia’s highly volatile political environment, the Prime Minister’s public statement had immediate consequences. Local actors scrambled to disassociate themselves from the trial. The Prime Minister’s language left little room for government officials to negotiate for the trial to be continued. It also sent a strong message to other countries where Tenofovir trials were being initiated. As Sou Sotheavy of WNU recalls, “We were negotiating with the researchers when the government said that the trial should be cancelled. When that happened we didn’t want to oppose the government. The Prime Minister is like our father when he says something is not good for us then we must agree with him.”²⁶

On 13 August, all work on the Cambodia trial stopped. Exactly why Prime Minister Hun Sen decided to make this statement and cancel the trial is unknown. The WNU received no communication from anyone in government about it. Some have suggested that the prime minister was concerned by the level of international press attention on Cambodia’s sex industry. Others have speculated that he was using the controversy surrounding the trial to take an action that disadvantaged political adversaries who had supported the trial.

²² Women’s Network for Unity press statement. “Women’s Network for Unity Protests Drug Trial Recruitment Tactics” 15 June 2004. available on-line at <http://www.wnu.womynsagenda.org/documents/wnu21june04.pdf>.

²³ Corinne Purtill & Yun Samean, *Hun Sen: Don’t Test Drugs on Cambodians*, Cambodia Daily, 4 Aug. 2004

²⁴ The Body.com, “Cambodian Prime Minister Joins the Push to Boycott Drug Trials”, 3 August, 2004, available on line at <http://www.thebody.com/content/art27148.html>.

²⁵ BBC News, “Major HIV drug trial to be halted”, 14 August, 2004. available on line at <http://news.bbc.co.uk/1/hi/health/3562704.stm>

²⁶ Interview with Sou Sotheavy, 21 June 2006.

The Aftermath

The sudden halt of the Cambodian trial preparations caught much of the research world by surprise. To the field as a whole, it constituted an abrupt and frightening precedent that immediately raised the stakes of the on-going debate around appropriate levels of community and civil society involvement in HIV prevention research. It also raised tensions in Cameroon where participant enrollment in the PrEP trial had started. A larger crisis appeared to be imminent and HIV prevention researchers were concerned about its possible implications for their own work. ACT UP/Paris agreed to refrain from further action on Tenofovir until December 2004 in order to allow time and space for negotiations to address the issues on the table. But no such dialogues were convened until 2005.

In 2004 and 2005, advocates had hoped for—and called for—the rapid creation of multi-sectoral opportunities to discuss the concerns that led to the trial preparations being halted in Cambodia, and later, the trial in Cameroon being suspended and eventually closed. This demand was a point of consensus amongst advocates who had otherwise widely differing views on the actions that led to the trial closures. However, almost a year elapsed between the closure of the Cambodia trial and the UNAIDS meeting in June 2005 that yielded a collective agreement on the need for widely-accepted standards for “involving the community” in clinical trial planning and implementation. The UNAIDS and IAS/Gates meetings in May and June of 2005 occurred too late to prevent the suspension of the Cameroon trial in January 2005.

Many participants at the UNAIDS June meeting were disappointed by the lack of clear-cut results and forward progress. The most visible output of the meeting was that, at the recommendation of the meeting participants, UNAIDS and the AIDS Vaccine Advocacy Coalition subsequently worked with a number of other organizations to develop guidelines for “Good Participatory Practice”²⁷. Presented as a living document, these guidelines were first published in November 2007 and are subject to ongoing development.

Meanwhile, the International AIDS Society and the Bill & Melinda Gates Foundation decided that another meeting to address the specific issues raised by the Cambodia and Cameroon trials was needed. This meeting occurred in May 2005 and was judged by its organisers to have been very productive.²⁸

The WNU, working with the Asian Pacific Network of Sex Workers, subsequently developed a code of practice for researchers entitled, “How to Work with Sex Workers: Code of Practice for Research and Questions for Researchers”.²⁹ This document is an important effort to clarify

²⁷ UNAIDS and AVAC 2007. Good participatory practice for biomedical HIV prevention trials, available on-line at <http://www.avac.org/gpp.htm>.

²⁸ Halima Y. Summary Meeting Update on Stakeholders Consultation to Address Issues Related to Tenofovir Prophylactic Research. PowerPoint presentation made in Rio de Janeiro, July 2005.

²⁹ Asian Pacific Sex Workers Network. “Making Sex Work Safe in Asia and the Pacific”, pages 23-24, available on line at <http://apnsw.org/apnsw.htm>

specific issues of concern to sex workers and prevent recurrences of the problems that arose in Cambodia.

The publication by UNAIDS of “Ethical Considerations for the Conduct of Biomedical HIV Prevention Trials” also represents significant progress.³⁰ But, clearly, more work is needed to develop a normative framework of procedures for HIV prevention trials that, by their implementation, will inspire confidence in trial host communities and researchers about how successful communication and collaboration around trial implementation occurs.



³⁰ UNAIDS. *Ethical Considerations in Biomedical HIV Prevention Trials*. Geneva, CH: UNAIDS; 2007. Available at http://data.unaids.org/pub/Manual/2007/jc1349_ethics_2_11_07_en.pdf

Chapter 2:

The Cameroon Experience

Calice Talom Yomgne³¹

Background

The proposed study of the use of Tenofovir to prevent HIV infection was to recruit 400 sex workers as trial participants in Cameroon. At the time of the proposed trial, Cameroon did not have a National comprehensive Law on Ethics in Biomedical Research such as the Huriot's law in France. There was however, a National Ethics Committee which at the time approved the ethical conduct of the study. This Ethics Committee did not, however, have an operating budget nor funds which would allow it to conduct site visits.

At the time this trial was to be conducted, the National ARV Program did not have Tenofovir as part of its main treatment line of antiretroviral drugs. Then, Tenofovir was expensive and no African programme could afford to include it as a first line drug. As at 2004/2005, the drug cost 336 Euros per month in France.

The beginning

Réseau Ethique Droit et Sida (REDS) found out about the proposed study while reading through conference abstracts of the IAS conference held in July 2003 in Paris where the result of prophylactic use of Tenofovir TDF in monkeys was presented. In 2004, the abstract was also published³². There was already information circulating about a proposed clinical trial involving the use of Tenofovir which was to take place in three African countries namely Cameroon, Ghana and Nigeria as well as in Cambodia and in the US.

REDS then got curious and started to seek for information about the trial. The group learnt from the Medical Center of Congo Area Two about preparations for a planned trial. Personnel were being trained for the trial on how to collect blood samples and obtain informed consent at the time of the initial contact with the hospital. I was then referred to the Site Coordinator of the study for further details and to collect a copy of the protocol. The Site Coordinator refused to share the protocol.

³¹ The Author works with Réseau Ethique Droit et Sida (REDS). REDS is an activist group established in Cameroon in 1998 aimed at promoting education, ethics and legal analysis of AIDS related policies. REDS is the Cameroonian branch of the African Network on AIDS Ethics and Rights (Réseau Africain sur l'Ethique, le Droit et le VIH), funded through UNDP in Dakar. REDS seeks to ensure that research being conducted, particularly on PLWHA, is legitimate. It liaised with Act Up Paris in this report. Act Up Paris, an NGO, was founded at the Gay Pride March in Paris in June 1989 to transform its members' anger about the AIDS epidemic into a political response. The Organisation advocates for the rights of all people with HIV and AIDS, for sexual freedom, and to give voice to those who are traditionally exploited and silenced. They also lobby and negotiate with government, pharmaceutical companies, and medical and research institutions for the good of PLWA.

³² Peterson L et al "findings from double-blind ,randomized,placebo-controlled trial of tenefovir disoproxil fumarate for prevention of HIV infection in women",THLB0103

Faced with this difficulty, REDS contacted Act-Up Paris through Fabrice Pilorgé and Regis Samba-Kounzy for help with respect to obtaining a copy of the protocol for analysis. Act-Up then sent some documents and specific information about the Nigeria component of the research. These documents sufficed since we learnt that the Cameroon and Nigeria study were similar and proposed by the same organization.

Analysing the protocol

In May, 2004, Regis Samba-Kounzy and Fabrice Pilorgé came on a field visit to meet with their Cameroonian colleagues who were members of the Pan African Treatment Access Movement (PATAM). Fabrice Pilorgé, Regis Samba Kounzy and Calice Talom, visited the trial site in Douala, and insisted on having a copy of the protocol. We finally obtained the protocol, the patient information sheet and the informed consent form. Back in Yaoundé, a team consisting of Jean Marie Talom, Calice Talom Yomgne, Regis Samba-Kounzy and Fabrice Pilorgé were constituted to study the protocol and documents received.

The team identified the following flaws with the protocol:

1. All the documents received were only written in English. The study was to be conducted in cosmopolitan Douala where there are English speaking people and French speaking people. It was important to us that the documents meant for the potential participants were produced in both French and English using simple understandable languages.
2. The absence of the female condom as part of the prevention package was a source of concern for the team. The trial planned to recruit girls with multiple sex partners. While HIV infection was the anticipated end point of the study, the study equally needed to take responsibility of not unduly exposing the girls to the risk of HIV infection. The team felt the research needed to provide the girls with all that they require to protect themselves such that if they do have unprotected sex , it would not be because they lacked the means to protect themselves but because they decided to have unprotected sex. The female condom was on sale in the country at the time of the study for 100 CFA a piece. Sex workers were complaining of difficulty in negotiating condom use at the time of the study. Providing both the male and the female condoms to trial participants could empower the girls knowing that they could wear the female condom prior to having sex.
3. The team was also concerned about the prospects of the trial participants having future access to the drugs if proven effective to prevent HIV infection. The protocol made no reference to this, neither was the team aware of any obligation made to the National Government to assure future access of trial participants to drugs if proven effective. The

team considered this a major violation of paragraph 30 of the Helsinki Declaration³³ which implied that when you want to conduct a trial amongst a vulnerable population, one must always protect that population and that when research is conducted in a context of extreme poverty that it is important to think about the benefits for the community. In other words, how would the trial participants benefit from this product if it is shown to be effective in protecting against HIV?

4. The team also noticed that there was no provision made for the care of HIV seroconverters in the protocol. This we considered unethical. The team found it disturbing that Gilead could provide Tenofovir and the placebo for free for the study, earn so much money from the sales of the drug and yet could not agree with Family Health International to include a clause in the protocol to assure HIV seroconverters in the study future access to care and treatment. The team then queried the ethical review process in the light of these findings and chose to review the ethical approval process for the protocol.

Consultation with National officials

The team visited the National HIV/AIDS Committee and met with the official who was providing oversight for HIV/AIDS trials in the country. He was not aware of the planned trial. The team also met with the Head of the Operational Division of Health (the Division was just newly constituted at this time) who noted that in view of the various flaws the team raised, he was sure administrative authorization of such a trial could not have been issued.

The team now divided into two - Regis Samba-Kounzy and Fabrice Pilorgé were to meet with the Head of the National Ethics Committee while Calice Talom Yomgne and Jean Marie Talom went to the Cameroon Health Program to meet with the Head of the NGO responsible for the logistics of this trial in Cameroon.

The Head of the National Ethics Committee stated that he did not recall that the protocol did not address medical care for HIV seroconverters; did not offer female condoms in addition to male condoms, and did not assure future access of Tenofovir to trial participants if found effective. He stated that if the issues raised are from the protocol then he did not think it was right; but he noted that he remembered being informed that care was to be provided for

³³ The Declaration of Helsinki was developed by the World Medical Association and adopted in 1964. It had since been amended in 1979, 1983, 1989, 1996, 2000. It was created to restore integrity to the medical profession with the initial focus being defining the physician's duties. The Declaration was motivated in part by desire for professional control of the research enterprise. They are principles, not rules and contain 32 short clauses with no elaboration. It is advisory in nature but recognized in national legislation and WHO practices

people who seroconverted. He offered to check up the details and get back to Regis Samba-Kounzy and Fabrice Pilorgé.

The Head of the NGO responsible for the logistics of this trial in Cameroon on the other hand issued threats when Jean Marie Talom and Calice Talom Yomgne shared their concerns about the protocol with him. He noted that ethical clearance had been received for the study from the National Ethics Committee adding that the team cannot make the research look bad. He further noted that there are no scientific studies that prove that the female condom protects, and it was new and so could not be offered in the trial. The team disagreed with this argument noting that female condoms were on sale in Cameroon and is being used around the world. He finally noted that he was not in a position to make changes to the protocol.

Consultation with researchers

Next, the whole team met with the Principal Investigator (PI) for the study. The meeting held in his office at the Gynecology-Obstetrics Hospital in N'gouso. The team shared the concerns about the study. He noted we had valid issues.

He agreed that French versions of the document did not exist and that the female condom was not included in the protocol during the study design because it was considered costly.

We argued against this noting that female condoms were on sale in Cameroon for 100 francs. Furthermore, the placebo and Tenofovir versions being used in the study are provided for free by Gilead pharmaceutical company. The female condom could be found in the US and in England. Why did the researcher not negotiate with the trial sponsors to make the female condom available for the trial? The PI further argued that the ladies (potential trial participants) were unfamiliar with the female condom and that its incorrect use could increase their HIV exposure risk. The team did not agree with this argument and noted that even the male condom which had been sold in Cameroon for many years, was still being used incorrectly. All the trial needs to do is train trial participants on correct use of both male and female condoms and counsel on its consistent use. Risk taking by trial participants should not be linked to unavailability of resources to protect oneself.

The team also raised the issue of care for HIV seroconverters. He noted that the study was not designed to resolve these problems and this is something that would be hard to change in the protocol. The team argued that Gilead had made huge profit from selling the product to people living with HIV in the developed countries. It was unacceptable that the product was to be tested for possible new use, effectiveness and efficacy based on HIV seroconversion, and yet the trial sponsors were not willing to ensure seroconverters get treated. This was something that needed to be changed in the protocol.

The PI noted he would contact Family Health International (FHI) to see how changes could be made to the protocol in view of the issues raised. He also agreed to translate the documents into French and ensure all trial sites have access to the French version of the documents. Female condom access and treatment of HIV seroconverters was to be discussed with FHI. He noted that the issue of future access to drugs was also not discussed but he would discuss this with the Government. For the team, these changes needed to be made to make the trial ethical. A final demand was the need for appropriate referral of those who test positive at recruitment to institutions who can provide care based on prior arrangements. These discussions held in May and recruitment for the trial was meant to start on June 15 2004.

Consultation with NGOs

The team met with other people because of the need to understand the degree of involvement of various parties. We went to Medecins Sans Frontières (MSF) and met with the Organisation's Chief of Mission because we knew that MSF had a program for ARV drug access at the Congo 2 Medical Center. MSF noted they were not engaged with the research.

The team also met with the Cameroonian Red Cross who was conducting HIV prevention and rehabilitation work with sex workers in Cameroon. The Red Cross was concerned about the trial being conducted with this population because of the possibility of trial participants having a therapeutic misconception. For them, it is important to stress this issue to the researchers so as to minimise the risk of HIV infection of the ladies during the course of the trial. There was a consensus on the need to advocate for protocol change but the Red Cross noted they could not be involved with this as they were an international organization.

The team consulted with AFASO which is an organization of women living with HIV who were also unaware of the trial and the fact that it would be focusing on women. SWAA Cameroon Centre division (National bureau) was also not aware of the planned trial.

Unfolding events

In July 2004, the team followed up on how the project was evolving. We realized that the study protocol documents were still being distributed exclusively in English. We learnt from the Site Investigator in Douala that the documents were still in the process of translation but recruitment had already begun.

Given that there were no efforts to effect protocol changes despite the raised concerns and consultation, REDS knew that more drastic measures had to be taken.

The International AIDS conference in Bangkok was approaching. REDS also had a meeting in Paris with Solidarité Sida prior to the Bangkok meeting. We took advantage of our stay in Paris

to visit the ANRS (National Research Agency on AIDS) where there were plans to present the results of their Triomune study. We met with our colleagues in Act-Up who were planning to produce a new edition of the newsletter called *Protocole Sud* (Southern Protocol) where they feature stories on ethical and unethical research in Africa. We requested that the oral Tenofovir study in Cameroon be reported in the newsletter for possible distribution at the upcoming Bangkok conference. The newsletter was to share the concerns of the Cameroon community about the unethical design of the trial.

The Bangkok meeting was an important forum to share information. Act-Up wanted to feature other things in their newsletter which they considered important. REDS advocated for the publication of the Tenofovir story because Cameroon's Health Minister and his entourage would be at the meeting. This was an opportunity for us to catch his attention.

A consensus was reached. Act-Up published a special issue called **Special Cameroon issue #2**. This version was published in both English and French. This was distributed in Bangkok and the Cameroonian delegation received this document.

In September, I went back to the trial centre in Douala and noticed that the patient information sheet and the informed consent form had been translated to French though they were not perfectly done, when compared to the English version by my assessment. Other things had not changed though.

Information had also started circulating around Cameroon about the trial: Those who had read the newsletter *Protocole Sud*, were sending mails to warn their families in Cameroon not to join the trial or allow female family members to join the trial. The heat was gradually warming things up.

Media consultation: On December 1st 2004 we decided to speak to the press. Jean Marie Talom gave an interview to "La Nouvelle Expression" and "Messenger." France 2, a French TV station, contacted Act-Up to find out about what was happening in Cameroon. They referred the TV station to REDS. I received a call from a journalist named Eric Colomer who noted he was interested in visiting Cameroon to discuss the study and to interview some of the trial participants. I agreed to an interview and linked him up with some trial participants.

I linked up with about 20 trial participants who had agreed to share with the journalists their motivations for joining the trial. In January 2005 France 2 aired the story as part of their televised series "Complement d'enquete" (Investigative Report) titled "What the pharmaceutical Companies don't tell us."

The aftermath: Immediately after the show was aired in January 2005, the trial became an instant scandal in Cameroon.

The Minister of Health announced that the study was ethical and there was no problem with the study. The Ethics committee of Family Health International came to Cameroon and made the same statement. We at REDS thought this was outrageous because the Ministry appeared to base its verdict on the report provided by FHI, the research organisation. Such evaluation could not be objective.

The Head of the National Committee on Ethics contacted the media and noted he was interviewed by France 2 but that his interview was censored. France 2 then went ahead to air the interview with him. This only created further discomfort about the trial in the public as it became glaring that the committee did not have an operational budget. The public perception of the interview was that the product was to possibly function like a vaccine.

The local media misinterpreted the France 2 report in so many ways: They assumed that the study product was a vaccine and that the study participants were being injected with the virus. REDS members made efforts to clarify the misinformation about the trial in the media. The fact that many of the reporters did not understand the science of the study gave room for biased reporting. Only the “Messenger” and the “Nouvelle Expression” wrote factual information about the trial.

The sudden upheaval that resulted from the media report scared members of REDS. The study team was also not interested in talking with us about the trial anymore. This bothered us. We continued to make frantic efforts to discuss and correct media misinformation but the media just focused on voicing the government’s position.

Radio Equinoxe in Douala agreed to do two interviews with REDS and these were broadcasted: one was a Sunday broadcast produced by Mr. Reinnier Kazé in which I highlighted the unethical issues identified in the trial and clarified how these were violations of the rights of the trial participants as outlined in the Helsinki declaration. These were the same issues raised in the second interview conducted by Suzanne Kala Lobe on the show ‘Polymous’. REDS was also interviewed by “Voice of America”, the BBC by *Jeune Afrique Intelligent* (Young Intelligent Africa), and by IRIN (the UN News Agency). Our discussion had consistently been on the need to review the protocol in view of the issues we considered unethical.

The local authorities started to consult about the trial. REDS planned to organize demonstrations in Yaoundé, Douala, and in Paris in consultation with our partners in Paris. The demonstration in Cameroon was later cancelled because there was a possibility that local authorities would misinform the population and use the public media to make political connotations to the planned street protests. The protest was then limited to Paris. Act-Up Paris

demonstrated in front of the Cameroonian Embassy in Paris. During the demonstration, some were beaten up by the police and some were hurt.

Two days after these demonstrations, the Cameroonian government asked the Health Minister to conduct an investigation into the Tenofovir issue. That was how the Peter Ndoumbé Commission came to be established. Peter Ndoumbé is a member of the National Ethics Committee and he was to preside over the investigative committee.

I, amongst others, were invited to speak to the committee. I honoured the invitation. A week after the commencement of investigations, the committee simply announced on the national radio that the study was suspended due to reasons of administrative dysfunction and serious gaps. No further explanations were provided.

The National Order of Medical Doctors of Cameroon also conducted an investigation and they listened to REDS and to some trial participants. The National Order of Doctors turned in the results of their investigation and clearly stated that there was both administrative dysfunction and ethical gaps in the design and conduct of the study.

REDS was informed that the research team had organized meetings with some community organizations asking them to sign a support statement for the trial. An organization called SUNAIDS reached out to REDS to ask if they should go ahead and sign the document. We advised that organizations were free to sign documents once their roles in the trial were clearly spelt out. Coastal SWAA was equally asked for partnership on the trial. REDS learnt they did not participate.

International deliberations

In May 2005, I received an invitation from International AIDS Society to join a meeting being organised in Seattle. The meeting had three objectives:

1. Bring together stakeholders engaged with TDF prophylactic-treatment research including Investigators, Study sponsors, Host Government representatives, developed world activists and policy-makers.
2. Identify the ethical and operational challenges that obstruct existing research and work towards the resolution of as many of these challenges as possible.
3. Identify strategies for ongoing problem management including reporting of emerging challenges to named individuals or agencies and mechanism for resolving these.

Anticipated outcomes of the meeting included an agreed action plan for the systematic redress of challenges associated with current TDF trials, and an agreed action for establishment of

ongoing dialogue between stakeholders including follow-up from stakeholder consultation meetings. Other key players in the controversy in Cameroon and other countries were also invited.

During the course of the meeting we made suggestions to the team. We outlined the problems because participants at the Seattle meeting wanted to have the information and understand what it was all about. When I presented the ethical problems that we had identified they asked us to work in a Cameroonian team. During the course of the meeting, the Cameroon team worked together to identify ways of addressing concerns. Once again, I raised all the issues of concern about the protocol.

The team agreed to translate all documents to French; refer those who test positive during recruitment to known health centers with whom the trial had established contact; care for people who sero-converted and developed liver problems during the trial; and draw a formal agreement with the National government to ensure Cameroonians benefit from the use of Tenofovir if found effective. All these requests were acceded to and included in the final meeting document.

During the FHI team presentation at the meeting, the focus was on the closure of the Nigeria study. FHI noted the study closure was due to the incompetence of the researchers. The community could not appreciate this and asked how the team could be considered incompetent when they, FHI, provided the needed training. The presenter also noted that they were not aware of the reason why the Cameroon trial was shut down. The Cameroon team found this unacceptable and noted that the report of the investigative team was submitted to FHI and the meeting was not about defending the un-defendable. Dr. Helen Gayle from the Bill Gates Foundation clearly noted that the objective of the meeting was to address problems, find solutions and work through ways to ensure the study can start again.

At the conclusion of the consultation, the Cameroon team was looking forward to further consultations in country to discuss with other stakeholders about the outcome of the international consultation, plans for protocol review and continuation of the trial. This never happened.

There were regional and international UNAIDS facilitated consultations on HIV prevention trials in Abuja, Nigeria where the lessons learnt from the Tenofovir controversy were shared. This was shared and discussed at the international consultation held in Geneva.

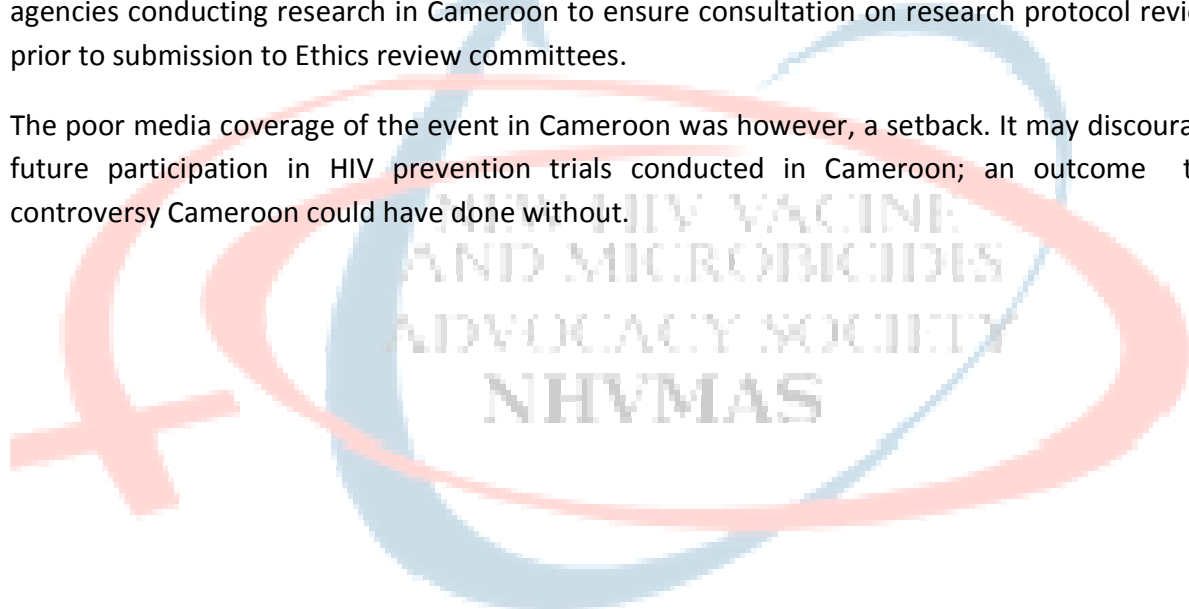
Unfortunately, nothing new came out for the Cameroon study and so the trial ended in Cameroon.

Final outcomes

Though the trial ended in Cameroon, the controversy had its positive outcome for Cameroon. REDS works better and more positively with the National government. The community of researchers and the government now see the organization as contributing to improve the process of research conducted in Cameroon.

The UNAIDS consultation also led to the development of the Good Participatory Practice document which should help to guide community engagement in HIV prevention trials. The document addresses the need to include care and treatment for people who sero-convert during a trial in planning for HIV prevention studies. This change is a result of sustained community advocacy. This process has also stimulated the interest and engagement of African Civil society in research. In Cameroon, there is now an inter-associative working group that addresses the protection of people who participate in research. The group works with research agencies conducting research in Cameroon to ensure consultation on research protocol review prior to submission to Ethics review committees.

The poor media coverage of the event in Cameroon was however, a setback. It may discourage future participation in HIV prevention trials conducted in Cameroon; an outcome the controversy Cameroon could have done without.



Chapter 3:

The Nigeria story Morenike Ukpong³⁴

The beginning

On the 26th of May 2004, the New HIV Vaccine and Microbicide Advocacy Society (NHVMAS) held its first National Advocates meeting.³⁵ The objective of the meeting was for members of the coalition to chart a way forward for the coalition over the next three years. Stakeholders involved with New HIV Prevention research and development – including past and present microbicide study Principal Investigators (PIs) in the country, ethicists, community advocates, policy makers, regulatory agency staff and journalists were in attendance. Also in attendance at that meeting was the PI for the proposed Oral Tenofovir trial to be conducted in Nigeria by Family Health International,³⁶ who presented information about the trial. The presentation generated numerous questions concerning the feasibility of using antiretroviral drugs (ARVs) for the prevention of HIV infection. Many of the issues discussed included the need to better understand the research protocol. Advocates were not comfortable with plans to conduct the research and long after the formal conclusion of the meeting, advocates continued their discussions about the need to better understand the research before they could consider giving it their support.

However, following the 2004 International AIDS Conference in Bangkok, a posting was sent to the Nigeria eforum - a listserv dedicated to the discussion of global HIV issues. The listserv is moderated by the Journalists Against AIDS (JAAIDS) Nigeria. The founding Executive Director of this organization, Omololu Falobi, was also the Co-Coordinator of NHVMAS and an active planner and convener of the National Advocates Meeting. The post to the listserv was made by a participant at the National Advocates Meeting who directs the affairs of a widely acclaimed sex workers network in the country. In her posting, she had inquired about the planned Nigerian PrEP trial in view of the controversies that ensued over the trial in Bangkok.

Omololu Falobi immediately got in touch with the second Co-Coordinator of NHVMAS, Morenike Ukpong (the author of this section of the report) and the PI of the trial in Nigeria. He shared the posting with both individuals and requested a response to the query from the local PI of the Oral Tenofovir study so he could post both the query and the response at the same

³⁴ The author coordinates the New HIV Vaccine and Microbicide Advocacy Society (NHVMAS) which was founded in 2003. The mission of NHVMAS is to ensure future access of Nigerians to New HIV Prevention technologies (NPTs) as soon as they are developed. It facilitates active engagement of Nigeria in NPT research and development through creation of a conducive environment for such activities.

³⁵ Report of this meeting is published in the NHVMAG report titled 'Setting the stage for New HIV Prevention Technologies in Nigeria' published by NHVMAG in 2004..

³⁶ Details of the research is in the report published by NHVMAG titled 'situation report on New HIV Prevention Technologies in Nigeria' in 2005

time to the listserv. The PI noted he had to get back to his International partners before he could respond. Omololu waited for the response which never came.

Two weeks later, the original post was re-sent and this time the author inquired as to why it had not been posted. The eforum moderator re-sent this query to both parties and noted that he could no longer hold back from posting if no response was received. Two days later, specifically the 30th of August 2004, the moderator posted the query. It read '*Gilead, the company that makes Tenofovir and which is part of a six-nation study, has been told to stop its tests in Cambodia after protests about unethical practices related to the study (see article below). We'd like more information about Gilead's trials in Nigeria and elsewhere in Africa*'. A report by BBC (<http://news.bbc.co.uk/1/hi/health/3562704.stm>) was cross posted. NHVMAS cross posted this to her moderated listserv. After the post was made, a very vigorous listserv debate began on the JAAIDS and NHVMAS listservs. The entire dialogue and its key themes are summarized in the first volume of the Oral Tenofovir series published by NHVMAS³⁷

The listserv based debate

Early in the dialogue, the NHVMAS Ethics Committee tried to get access to the protocol so that the committee could review it in order to better understand what the trial would involve. It obtained a copy of the Cameroon trial protocol - which was believed to be the same as that of the Nigerian study - when one of the committee members liaised with a friend in France who was aware of the Cameroon Oral Tenofovir controversy and had links to the advocates actively involved with investigating the Cameroon trial.

A copy of the protocol was sent to the Chair of the NHVMAS Scientific Committee to assess the scientific integrity of the research. The Ethics Committee then took time to review the ethical issues and community concerns regarding the conduct of the trial. The Scientific Committee Chair sent the protocol out to and colleagues outside the country for review and comments.

The Scientific Committee wrote back to the Ethics Committee and NHVMAS secretariat that the methodology and design of the trial was scientifically appropriate to answer the research question. The Ethics Committee however raised a number of issues and wrote to the Research institution on the 26th of September, 2004 noting the following:

Recommendations made include:

1. The need for trial participants to receive the BEST possible care in this research process. There should be no compromise.

³⁷ Details of the dialogue are contained in the report published in 2005 by NHVMAS titled 'Oral Tenofovir Controversy'

2. The research protocol should also be amended to include:
- a. Interventions to ensure community preparedness on the part of the researchers. Members of the community within the trial focus area should be adequately prepared for the trial (informed and kept updated about the research) so they can give their support for the process in view of stigma related to HIV infection. Where the community is not adequately prepared, there is a possibility that myths and misconceptions would develop about the trial. Trial participants' retention may then be difficult. In a bid for researchers to then meet deadlines in view of funding constraints, compromises may then start to occur in the trial design and volunteer recruitment procedure. The Provost of the College of Medicine observed that the TDF study was preceded by formative research. While we genuinely appreciate these steps, NHVMAS stresses that community preparedness, as internationally practiced, is much wider than what the Provost outlined, and remains a priority need.
 - b. Future dialogue should include interested community advocates. We do support the need for regular community meetings to review progress and problems, but please include community members who are vast on the issues on the Board. NHVMAS suggests that the community should be represented on the Clinical Monitoring Team, the Safety Monitoring Team, the Data Monitoring Committee and during the UCH IRB monitoring and review process. We would not want a compromise on this. This would ensure that that the community views, perspectives and concerns are addressed during deliberations and in the decision making process. The community members would then report back to the community and such representatives would be our liaising arm of the project. The community could confidently relate to their reports.
 - c. The protocol should be more humane and try to address the health needs of trial participants who enrol on the trial. All health problems that arise in the course of the trial, whether trial related or not, should be adequately addressed. Specifically, female condoms should be included in the trial's prevention package, HIV seroconverters should be ensured access to treatment, and those that screen out of trial should have facilitated access to treatment. Given the health profiles of poor Nigerian women, NHVMAS argued that if Grade 3 or 4 adverse occurrences are considered unrelated to the study drug, researchers should discontinue the study drug regardless. Also, data on interaction between malaria and HIV was important as identified in the justification section of the protocol.
 - d. All recommendations should be reflected in the protocol and informed consent form that trial participants are to sign.
 - e. The College of Medicine believes that Tenofovir (TDF) is a safe drug for use as a chemo-prophylactic against HIV infection following the result of phase 1/II in literature. The Provost particularly noted that a number of Phase 1 studies on TDF have been conducted in HIV negative participants, including studies on drug interaction, renal impairment and the drug's pharmacokinetics (studies GS 909,

914, 919, 930, 932, 943 and 1037). The studies noted that abnormalities, including elevated creatinine phosphokinase and liver functions tests. However, these were resolved with or without drug discontinuation and without sequelae. To detect these changes for the present research, blood samples would be taken from the participants at screening, enrolment and at follow-up. Abnormal liver and kidney tests form part of the exclusion criteria and information about the possibility for these side effects has been included in the screening and enrolment consents to be given to the participants.

NHVMAS could not however find published peer reviewed reports on the study of Tenofovir use in HIV sero-negative individuals during its literature search. We note that the phase I safety trial reported in the literature was done amongst HIV-positive people, not HIV-negative individuals.³⁸

- f. **Establishment of a Community Advisory Board (CAB):** The Provost felt that establishing a CAB does not necessarily translate to community consultation and CAB has the potential for fuelling demands by some privileged members, which may not necessarily translate to community needs. While NHVMAS appreciates this concern, we believe that constitution of a genuinely-representative and functional CAB is a priority need. Aside from the fact that establishment of a CAB is a standard international requirement for any research study involving human subjects, NHVMAS believes that a CAB is necessary to provide the critical linkage between science and community in a way that goes beyond the duties assigned to a single individual. We intend to continue to discuss with the study team on the need to put this important structure in place.
- g. **Design and implementation of community preparedness activities at trial sites:** Community preparedness is a very important aspect of any research trial taking place within a human population. It includes community education and empowerment initiatives, sensitization programmes and identification of community needs relevant to the research effort. This will not only ensure support for the trial but would help increase the prospect of drug uptake in the future. Activities to ensure community preparedness for a trial is standard practice worldwide.

Fueling the controversy

On the 10th of September, 2004, the Head of the Institution where the research was being conducted responded to some of the issues raised during the debate. He noted that the trial was approved by the institutions ethics committee and that '*science is not*

³⁸ Patricia Barditch-Crovo, Steven G. Deeks, Ann Collier, et al. Phase I/II Trial of the Pharmacokinetics, Safety, and Antiretroviral Activity of Tenofovir Disoproxil Fumarate in Human Immunodeficiency Virus-Infected Adults. *Antimicrob Agents Chemother.* 2001 October; 45(10): 2733-2739).

and should not be conducted on the pages of newspaper or other related media'. This fuelled reactions from the advocates' community which included concerns about:

1. Monitoring and ensuring the rights of the research participants.
2. The critical importance of community engagement in research and that *'issues of scientific processes with impact on public health should be subjected to rigorous debate by interested public-minded stakeholders. The perception of science as a sacred masquerade whom only a restricted circle of anointed acolytes can view, is no longer acceptable. Epidemics such as HIV/AIDS and tuberculosis have taught us that community engagement is as important - perhaps even more important than - science in driving a solution. Informed discussion on ethical conduct lies NOT only in the realm of science. But we accept that the conduct of science should remain true to the highest demands of sobriety, objectivity and integrity'*
3. The community benefit from the trial as noted by one of the contributors to the debate: *"Finally, what benefit would the research be if at the end of this Phase II/III trial, Tenofovir is found to be effective in preventing HIV infection when taking daily as an oral pill, yet studies show that people do not consistently take daily medications for various reasons (even for treatments how much more for prevention!). Not all trials have to be conducted; conducted trials have to be to the benefit of all."*
4. The IRB's capacity to review the protocol as expressed by a contributor to the debate: *"I believe in the efficiency of the IRB in Ibadan but we are all learning. All the IRB members are not experts on new HIV prevention technologies. There are more community advocates that are better informed and so there is a place for public debates."*

Concluding the listserv discussion and the aftermath

On the 11th of October 2004, the listserv moderator brought discussions on the PreP study to a conclusion by summarizing discussions on the forum and continuing dialogue with the research institution directly.

Morenike Ukpong visited the research institution and dialogued with the local research PI and the Provost of the Medical School of the research institution. The research institution then convened a roundtable to discuss the recommendations about the protocol and informed NHVMAS that they had taken a few actions. These included the appointment of a Community liaison for the trial and the recommendation that the trial include assessment of malaria infection during patient follow up amongst others. The actions were recommended to FHI. Ironically, the Provost noted that none of the recommendations were implemented.

For unknown reasons, the study was temporarily closed late in 2004. In January 2005, the trial resumed without any consultation with the community. NHVMAS Steering Committee then proposed to document and share its concerns with NAFDAC (the drug and regulatory agency in Nigeria). While in the process of doing this, NHVMAS received a report that the Nigerian arm of the trial had been shut down and would be discontinued due to the inability of the local research team to adhere to the protocol and maintain good clinical practices.

On NHVMAS's part, the reasons for the trial closure seemed questionable. The community was indeed interested in dialoguing with the research team on how to improve the conduct of the research and NHVMAS made attempts to facilitate this discussion. A dialogue was never held. Advocates were suspicious that FHI must have learnt of its plan to inform NAFDAC of its concern with the trial and were proactive in shutting down the trial so as to prevent another public announcement of a shut down by National authorities.

NHVMAS wrote FHI to share its concern about the public announcement of its shut down of the trial, its impact for the country and the researcher in question and its failure to dialogue with stakeholders to address concerns prior to and after the closure of the trial.

Post trial consultation

NHVMAS was invited for a Bill and Melinda Gates Foundation sponsored discussion on the Oral Tenofovir controversy in 2005. Unfortunately, NHVMAS representative, Morenike Ukpog, could not attend the meeting due to her inability to secure a visa. After that, NHVMAS facilitated a National dialogue on HIV prevention trials with funding support from Global Campaign for Microbicide; co-facilitated a West and Central African meeting with UNAIDS and attended the UNAIDS convened international meeting on dialoguing around HIV prevention technology. The development of the Good Participatory Practice Guideline was the final outcome of these multilayer discussions and the seeming end of the dialogue around the controversy.

Events after the trial

The controversy that ensued around the PreP trial did leave its impact in Nigeria. There was high level of community engagement of the local PIs engaged in the SAVVY and CS3 trials. Multiple community and New HIV Prevention Technology (NPT) research PI consultations held at various times in country with these PIs actively engaged with community education and research literacy efforts.

Capacity build during the controversy also helped position NHVMAS well enough to continually serve as a community watch dog for not only NPT trials but also for HIV related trials in the country.

NHVMAS continues to play its role as a strong advocate for community engagement in NPT trials in the country, Africa and internationally. It sees itself as a watchdog for the ethical conduct of clinical trials in Nigeria while it continues to engage actively in regional and international discussions about NPT so as to ensure prompt future access of Nigerians to new NPT when developed.



Chapter 4:

The Thailand story

Karyn Kaplan³⁹

The beginning

In September, 2004, drug user activists from Thai Drug Users' Network (TDN) and other organizations were contacted by researchers conducting the "Bangkok Tenofovir Study"⁴⁰, a US Centre for Disease Control (CDC) sponsored phase II/III, randomized, double-blind, placebo-controlled study of the safety and efficacy of chemoprophylactic tenofovir (TDF), administered orally once daily to injecting drug users (IDUs) attending methadone clinics in Bangkok. On September 30, these community advocates, representing organizations including TDN, Thai AIDS Treatment Action Group (TTAG), and Population Services International (PSI) attended this first meeting with the Bangkok Tenofovir Study researchers (working through the Thai-US CDC Collaboration) at their offices at the Ministry of Public Health (MOPH).

At this first meeting, the trial researchers proceeded to inform the community advocates about the trial; they seemed open in wanting to accommodate concerns and requests. However, it quickly became evident that the trial researchers were unwilling to revise the protocol or alter fundamental design components despite requests made by community representatives at that meeting. These actions confused community representatives over the very point of opening up a dialogue initiated by the researchers. Community representatives were told that the protocol had already been submitted to the institutional review boards required for the trial, and at best, an amendment might be made on a specific topic later; but at this juncture, nothing could effectively be done to alter the protocol. This was a shock to the community advocates. "Why weren't we brought in earlier?," some thought.

One of the initial and main problems raised by the community at that first meeting and every subsequent encounter between community and researchers was the sub-standard prevention package offered by the trial. Other PreP study sites around the globe provided the highest standard of prevention care including condoms and counseling to participants. But in Bangkok, which was the only intravenous drug user (IDU) trial site, the study subjects were denied clean injecting equipment - the equivalent evidence-based standard appropriate for this study

³⁹ Thai AIDS Treatment Action Group (TTAG) was founded in 2002 to promote access to HIV/AIDS treatment for highly marginalized groups. TTAG, with a staff of 10 in Bangkok and Chiang Mai, works to promote equal access to AIDS treatment for all through policy advocacy, coalition-building, and strengthening the capacity of people living with or highly vulnerable to HIV/AIDS to advocate for their human rights. It focuses on expanding access to treatment for incarcerated populations, and to educate and empower people living with HIV/AIDS to access HIV prevention and treatment in their communities. TTAG works largely with rural poor and marginalized urban populations. It also provides direct services including meals, access to health care, support groups and HIV prevention tools at a drop-in center in Bangkok.

⁴⁰ Study of the Safety and Efficacy of Daily Tenofovir to Prevent HIV Infection among IDU in Bangkok, Thailand ("Bangkok Tenofovir Study")

population. This remained a constant point of contention, and trial researchers claimed they would bring this request to the PI, but in fact stalled on providing a clear answer. During ongoing negotiations from October – December 2004 leading up to the dissemination of an “open letter” by the Tenofovir Community Working Group to mainly US CDC trial researchers, the Thai and US researchers claimed that due to the US “ban on the use of federal funds to purchase needles,” combined with the Thai reluctance to provide them, clean needles would definitely not be provided. Community allies such as MSF-Belgium/Thailand offered, at one point later on in negotiations spilling into 2005, to act as a “third-party provider,” but even this proposal was not accepted.

Other issues raised included the lack of community representation on the “Community relations clubs” (CRC), which was set up “in order to establish mechanisms to solicit and respond to community attitudes about study procedures, the reputation of the study in the community, and questions arising from participants or the general community.”⁴¹ The CRC was originally set up under an earlier trial, the AIDSVAX B/E vaccine, also conducted among IDU attending Bangkok Metropolitan Administration (BMA) methadone clinics by the same PI on the TDF PREP trial, Dr. Kachit Choopanya of Taksin Hospital in Bangkok. TDN and TTAG argued that key community organizations working with this extremely marginalized, criminalized IDU population, including their groups, Center for AIDS Rights (CAR, now Foundation for AIDS Rights, or FAR), Thai Network of People Living with HIV/AIDS (TNP+) and others, would be a positive addition to the CRC.

A debate between the community and researchers over who constituted “community” was never resolved: while advocates felt the protocol’s description of community was suitable and identified them as possible members of the CRC or CAB, the researchers refused to recognise advocates as community. The trial researchers never allowed any of the community advocates from the Tenofovir Community Working Group⁴² into their meetings, whether as advisors, educators, or advocates on the CRC. Yet individual CRC members – these were often hand-picked IDUs from each of the various methadone clinics involved in the study - clearly lacked understanding on human rights, HIV, and ethics. Community advocates such as TDN and TTAG argued that this was not empowering the IDU community, but rather undermining the ability of community representatives on the CRC to truly be the voice of the participants; and such seats on the CRC required understanding and advocating on issues relevant to their rights in the trial.

A large part of the problem was a conflict of interest perceived by TDN, TTAG and others: trial recruiters were the very same people (often nurses) providing methadone at the clinics! This created a very untenable situation for fair recruitment. Later on in the anti-trial advocacy

⁴¹ Excerpts from “Bangkok Tenofovir Study” protocol, page 18.

⁴² Composed of: Thai AIDS Treatment Action Group, Thai Drug Users’ Network, Thai NGO Coalition on AIDS, MSF-Belgium/Thailand, and Center for AIDS Rights (now Foundation for AIDS Rights).

(discussed below), trial participants themselves described their inability to say “no” to the trial recruiters when pursued to join the trial. Trial participants repeatedly described feelings of “Kreng jai,” or “not disturbing others’ activities,” rendering them unable to refuse a request, especially when it is made by a nurse from whom they currently or formerly received methadone treatment - someone higher in the social hierarchy. This problem of the sense of obligation was further compounded by some recruiters using aggressive tactics such as calling a client or former client repeatedly at home, asking them to “help” her reach her quota (and bring friends); some of those approached were either no longer injecting or no longer clients at the clinics. In interviews with Tenofovir Community Working Group members, and later in direct testimony to trial researchers on January 31st, 2006, the final negotiation attempt (described further below), trial participants reported that under this duress, non-injectors, not-current methadone clients, and other people who did not actually fit the criteria were nevertheless recruited. The extent to which these significant problems were admitted by recruiters or known by researchers remains unknown.

Numerous other issues were raised by TDN and others over time, including several concrete ideas suggested on changing the trial protocol as well as demands to immediately halt the trial to enable rectification of the protocol as protocol implementation was still in its early phase of trial participant recruitment. The raised concerns were related to trial recruitment, enrolment and appropriate HIV counseling for drug users by specially-trained counselors or peers, the development of an effective referral and screening-out system, access to HIV-related services and treatment, including post-trial care; community role in educating and supporting an informed study population; post-trial drug supply negotiation, and training ideas and support including harm reduction for trial staff. Nothing the community advocates proposed was accepted; and even though the protocol was still in the pre-approval stage, the trial researchers flatly refused to halt or delay recruiting, incorporate community concerns or proposed changes into the existing protocol.

After numerous failed community-researcher meetings, considerable resistance to substantive changes proposed by the community, as well as adamant denial by researchers of ethical wrong-doing, TDN, TTAG and others started going public with their accusations and frustrations. An open letter to the trial sponsors was read out at a CDC meeting in Atlanta⁴³; opinion pieces were written by community advocates and supportive groups like MSF-Belgium/Thailand and published in journals such as *The Lancet* and *PLoS*⁴⁴, as well as other publications addressing perceived ethical violations^{45, 46}; appeals by community to UN agencies

⁴³ Open Letter to the US Centers for Disease Control (CDC) From the Thai Drug Users' Network," July 24, 2005; Letter to Thailand Tenofovir PREP Study Researchers," Tenofovir Community Working Group, 8 December 2004 (original in possession of author)

⁴⁴ Open Letter to the US Centers for Disease Control (CDC) From the Thai Drug Users' Network," July 24, 2005

⁴⁵ http://www.soros.org/initiatives/health/focus/ihrd/articles_publications/publications/delivering_20060801/delivering_20060724.pdf, page 177, “

such as UNAIDS⁴⁷, Bangkok government officials including the Deputy Governor⁴⁸, and others were made by the community in an effort to have their mounting concerns addressed productively.

Meanwhile, community representatives dedicated significant time to educating the study participants in ethics and rights, in order to improve their understanding of the trial, their rights, and the larger context of HIV prevention research, as many of the study participants accessed services run by TDN, particularly their harm reduction drop-in center.

Finally, the community advocates from Thailand joined international meetings to address problems in numerous TDF trials across the globe, including meetings held in London, Seattle, Geneva and Thailand. These meetings were hosted by numerous stakeholders including the Bill and Melinda Gates Foundation, UNAIDS, AVAC and others. Unfortunately, these meetings did not resolve the immediate problems facing the current trials but focused on urgently thinking about how to preempt problems and improve collaborations in future trials. It is important to note however, that these efforts to broach topics of community/researcher divides and ethical problems in prevention research led to the development of a new set of guidelines, the “Good Participatory Practice” document that is a unique researcher/community collaborative document.

Protest/Outcome

Among the community advocates (self-appointed the “Tenofovir Community Working Group” -- TDN, drug users, CBOs/NGOs), there was a split that was never successfully resolved *vis a vis* the trial. Some wanted to stop the trial, citing ample evidence supporting their case that the trial was unethical and irresponsible, violating numerous ethical codes and guidelines. Others were trying desperately to believe in the possibility of a positive outcome, the “win-win” situation⁴⁹, despite repeated rebuttals from researchers and their claims that some of the advocates were simply “celebrity seekers.” There was a street protest by TDN, (picture attached) and attempts to educate and learn from other community groups in other countries who were experiencing similar problems in the context of their TDF PREP trial.

⁴⁶ Jintakarnon, S, Nakapiew S, Tienudom N, Suwannawong P, Wilson D. Unethical clinical trials in Thailand: a community response. Lancet 367 2005. 1617-1618

⁴⁷ On March 3, 2005.

⁴⁸ In May 2005.

⁴⁹ This was the Tenofovir Community Working Group’s goal from the outset (“win-win,” first articulated by Paisan Suwannawong at the initial September 30, 2004 meeting with trial researchers), meaning that the trial researchers enjoy active support by, for example, TDN by helping with peer education, counseling and advocacy on Tenofovir and trial-related issues, and the Working Group is supported by the trial in working together toward improved services for people who use drugs in the health care system, since the trial researchers prided themselves on ostensibly offering an “enhanced” quality of health care services to trial participants.

At the final meeting of trial participants, on January 31, 2006, community advocates and trial researchers (held at Taksin Hospital - the office of the PI), the Tenofovir Community Working Group tried one last time to make their case concerning numerous and increasing problems coming to light about the design and conduct of the trial and staff, as well as the lack of meaningful community involvement. At this meeting, more evidence was brought forth, including the fact that non-injectors had been recruited into the trial, that many participants did not understand the trial or their rights, and that a significant number of participants were not in fact swallowing the TDF (or placebo), but rather either storing it because they were not confident that it would not harm them, or because it could also be more valuable as an ARV. Moreover, the Working Group brought in "Patient Zero," who bravely described to the Thai-US CDC research team, PI and numerous trial staff that he felt coerced by recruiters into participating in the trial.

These misconceptions were not addressed by the trial staff or researchers, who claimed to be unaware of problems such as these. Community advocates were equally concerned that these unaddressed issues would impact negatively on the quality of the data collected and could be characterized as "dirty", inaccurate data, due to problems with recruitment methods, and some information obtained through unethical and controversial circumstances. Tenofovir Community Working Group discussions with study participants revealed that many study subjects had been kept on the trial without notification on study extension plans - years past the one-year original study timeframe- and had not been duly informed about when they could expect to stop having to take TDF.

One participant who had been in the trial for three years, noted that he had no idea why he was still being asked to take the TDF, nor when the trial would be over. There were community concerns about the possible effect of long use of products for those in the active arm of the study. When a few participants were asked why they continued in the study despite the clause in the informed consent form that noted that there were free to leave the trial at anytime, many cited the money received for reimbursement as an important motivator to continuing to participate in the trial, despite the significant lack of understanding about it.

The researchers offered only one significant role to members of the Tenofovir Community Working Group to participate in the study, which was to help improve the informed consent process. The Group chose not to work in this capacity, rejected the role, and from that moment on, there has been no formal communication between the researchers or the community advocates.

What could have been done differently and why

Within the Tenofovir Community Working Group, there was tension over whether or not to publicly protest and try to halt the trial as concerns about the implementation of the trial grew.

While many representatives, mainly the drug user activists, were adamant that the evidence of unethical research conduct and other violations warranted the canceling of the trial, others NGO advocates wanted to give the trial researchers a final opportunity at that Taksin Hospital meeting. Expectations included the possibility of researchers showing they valued the study participant concerns and community perspective, enough to make substantive changes to the protocol implementation process. This should include the inclusion of a third-party needle provider for the project, stopping the use of methadone providers as trial participant recruiters, and allowing Tenofovir Community Working Group representatives to participate on the Community Relations Club.

Once it became clear that the researchers would not address many of the raised concerns, none of the community advocates wanted to waste any more time talking or negotiating.

Perhaps we should have appealed directly to Gilead; perhaps we could have tried to stop the trial from the very beginning. However groups continued to provide peer-driven harm reduction services, and counsel study participants with problems and concerns. They were also directed to the “Community Liaison” officer, a “compromise” hire that the researchers made in response to our argument that there was no independent mechanism by which participants could voice their problems or concerns. The “Liaison” idea was not a request from the community but rather an effort of the researchers to provide more support to trial participants as a result of our complaints.

Various individuals and organizations from the now-defunct “Tenofovir Community Working Group” continue to educate and advocate for the respect of the fundamental human rights of people who use drugs, comprehensive harm reduction services, and increased community involvement in research as an ethical imperative for the conduct of HIV prevention clinical trials. Whether the goal is reached in this trial or the next is not entirely in our power; yet we will continue to actively advocate for these principles, programs and policies, and try to hold the relevant stakeholders accountable while we ourselves are constructively engaged.



Members of the Thai Drug Users Network (TDN) during the protest march.

Chapter 5:

The Malawi Story Edward Chigwedere

Introduction

This report outlines bits and pieces of what is understood with respect to the TDF trial in Malawi. It should be noted from the onset that this report has been written based mostly on anecdotal information around the trial. Ethical approval for a study to follow up the TDF study in Malawi was considerably lengthy. There are therefore so many loose ends you will find in the report that are certainly going to be tied as we explore the TDF trial in Malawi at a later date.

The bits and pieces about the trial in this report were gathered from *Protocol No 302, Formative Research in Support of Phase 2 Extended Safety and Effectiveness of TDF for HIV infection (which was read in less than 30 minutes because at the time of this report, the study team had not received an official approval to review the TDF study)*, a disapproval letter for the conduct of a Phase 3 PreP and discussions with a few people who knew about the trial.

The proposed study of TDF as an oral prophylaxis for the prevention of HIV infection in Malawi was planned to be conducted under the University of North Carolina (UNC) Research Program. UNC Research Program is a collaborative research institution between University of North Carolina and Kamuzu Central Hospital. Kamuzu Central Hospital is a referral hospital situated in the capital of Malawi, Lilongwe. The UNC program is housed in the Lilongwe Central Hospital premises.

The Malawi PreP trial

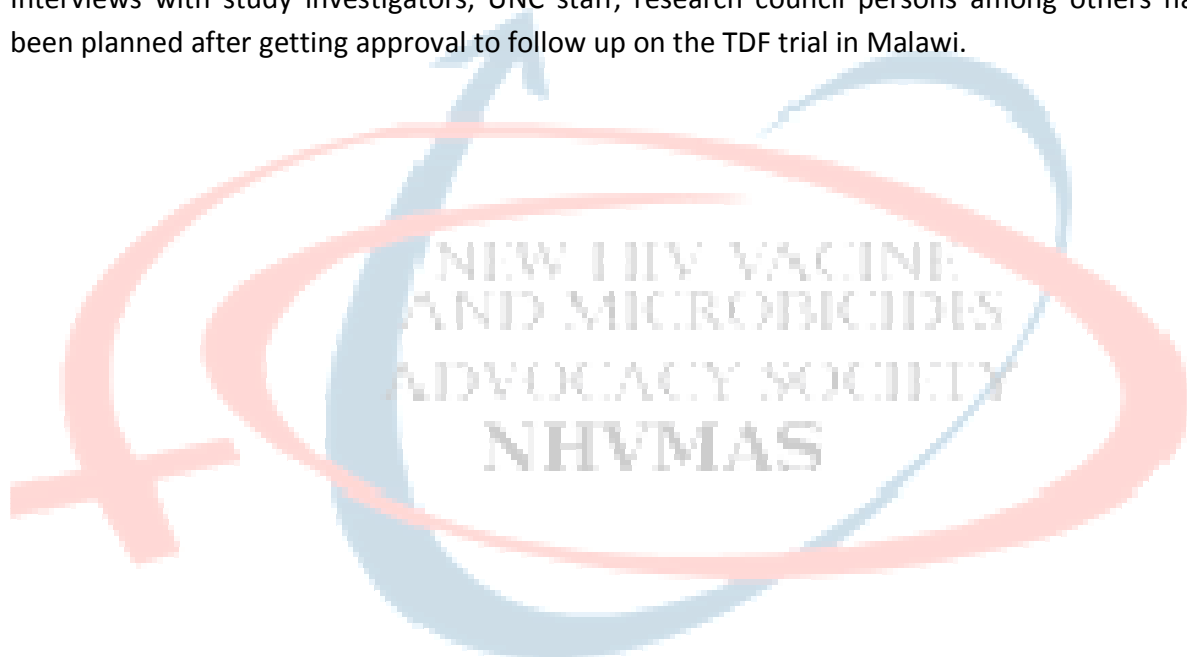
The phase II PreP study was approved in 2004. An approval letter was written on September 7, 2004, after the IRB had met on June 6, 2004. This approval came after UNC noted that the study team had “*addressed earlier raised queries*”. The queries were related to possible development of TDF resistance by trial participants and issues around data analysis. The details of the real issues raised on each of the queries and how they were addressed remain unclear. What however remains evident is that the June 16 2004 IRB meeting saw the issues they raised as minor and not warranting a total disapproval of the proposal. It is likely the committee wrote UNC advising them to address the aforementioned queries before the proposal could be approved.

Upon approval of the proposal, the formative research commenced. I was informed that the main focus of the formative research was *acceptability* of the TDF trial in Malawi. It is reported

that ninety (90) brothels/lounges/bars were identified and sex workers had already been identified who were going to recruit fellow sex workers into the trial.

On November 24, 2005, about 14 months after the approval of the proposal, the IRB chair wrote a discontinuation letter to UNC. Reasons for discontinuation are, again, not very clear. The IRB chair cites *“advice received from specialist HIV management group of the Ministry of Health (MoH) and a presentation on TDF from UNC on 18 November 2005.* Attempts to get information on what the advice from the MoH was and what the presentation at UNC covered (to prompt such a sudden turn of events) are still in progress. It remains intriguing understanding what prompted the MoH to give this advice. The phase II PreP study was thus, discontinued before initiation of the study sites.

Interviews with study investigators, UNC staff, research council persons among others have been planned after getting approval to follow up on the TDF trial in Malawi.



Chapter 6:

Analyzing the events

A review of the report of the controversies trailing the Tenofovir trials in these countries did highlight a few commonalities. These include the following:

- 1. Communities in each country organized themselves:** The primary actors in the discussions around the Tenofovir trial in each country were the communities themselves. These communities were organized and had advocates prior to the commencement of the trials in the countries. All the actors in each country did seek external consultations but the actions and reactions were primarily by the country based advocacy groups. It is offensive to insinuate that the reactions about the trial were instigated by external parties. It would be important for researchers to identify and engage these organized community of advocates in countries of proposed research in future studies.
- 2. Communities have channels of communication:** The communication channels between communities are effective and fast. Researchers or external parties to such organized communities may not readily identify or have access to these channels of communication. Communication with trusted NGOs to create space for bi-directional communication is critically important and would be helpful in future trials.
- 3. All groups requested for protocol change:** It is evident that the discontinuation of the trial was a decision made by the research team. No country requested for trial discontinuation. All actors in the controversy requested for a review of the research protocol so that it takes cognizance of their concerns which was not adequately addressed in the early versions of the trial. The importance of early community participation in research protocol development is well recognized and reiterated in the Good Participatory Practice Guideline (GPP) document and the Ethical Guidelines for Biomedical HIV Prevention Research.
- 4. Concerns about scientist and research handling of 'Communities' suggestions:** All engaged communities felt that their suggestions, concerns and inputs were not regarded as important by the researchers during the many discussions held between the two communities (advocates and researchers). Their views and perspectives were handled with levity. When suggestions were made that were not in line with the views and perspectives of the researchers, the research team often treated these suggestions as though they were based on inadequate education, information and understanding of the research. This was a concern identified in all the communities.
- 5. Lack of trust in the ethical review process:** While researchers seemed to have a lot of trust in the ethical review process (the ethical clearance of researches appears to be legitimate

reasons for the conduct of the research which is considered ethical in any community), communities often expressed lack of trust in that ethical review process. This may not be unconnected to communities not understanding how the ethical review of protocols are conducted; and the absence of a bridge between the community and the IRB. Ethical approval of a protocol may therefore not be enough to gain community confidence in a research process. Dialogue with the community is equally important.

- 6. Informed consent comprehension:** Comprehension of the information provided during the informed consent process was important for meaningful participation of the research participants. Ironically, the communities in which these trials were planned were research illiterate. The time frame for the conduct of the research was too short to ensure research literacy which is a basis for adequate comprehension of the informed consent document; and to facilitate meaningful participation of trial participants in research. This also gives room for the possibility of therapeutic misconceptions especially when these trials take place within health care providing institutions. What is the implication of this? Should trials be conducted only in research literate communities? If so, is there a possibility for research fatigue in communities where research is continuously conducted? How do you ensure adequate time is spent to facilitate research literacy in low literacy communities?
- 7. Access to treatment:** The researches were planned to be conducted in resource poor settings amongst marginalized communities. Access to health care was poor in these communities. Health Insurance was non-existent. People had also learnt about the many side effects associated with the use of ARVs by HIV positive individuals. The possibilities of these side effects in HIV negative individuals were also real. Communities therefore raised concerns about access to immediate and future care of trial participants who developed health problems, care for HIV seroconverters, as well as care of screened out trial participants. Concerns about present and future access to trial injury related care was therefore a huge concern.
- 8. Lack of safety data:** All actors in the controversy were unhappy about the lack of sufficient animal data and complete absence of a phase I study prior to the conduct of a phase IIb trial. The scientific basis for the conduct of a phase IIb trial in developing countries without adequate data from phase I and animal studies contravenes the science taught by the same science community. When and why did the rules of scientific conduct of clinical trials change? Who changes rules? These concerns were serious enough for the communities to feel very suspicious of the research, its intent and thus the need to ensure maximal immediate benefit from the research than promises of future reward
- 9. Inability of local researchers to speak and act around the trial:** The inability of local researchers to respond promptly to issues and questions raised by the communities were

also a source of concern. Their untimely response did exacerbate the crisis. Much more than that, the constant response on the need to discuss simple issues with their international partners before taking simple decisions only made the communities perceive that the trial was entirely controlled by foreign actors who were less sensitive and conversant with local needs and peculiarities. The treatment of the local PIs as simple data collectors was also not very well received.

10. Advocacy/Networking: Communities formed linkages with other groups that know the issues to help interpret, demystify the protocol and forge alliances for action. These efforts resulted in other outcomes which did include collaborations and raising of common platforms for actions.

11. Media Engagement and the important role it can play in shaping public perception about research: All the countries except Malawi, reported exploring media opportunities (newsletters, radio interviews, listservs) as a means of sharing information, drawing the attention of the public/ policy makers, and putting the issue on the front burner of public discourse. This negates the researchers' perceptions (as stated in the case of Nigeria) that science should not be discussed on the pages of newspapers/media. The reports also raise the issues about how "bad press" and negative media outcomes can influence the outcomes and perceptions about a clinical trial and raises concerns about the best way(s) to manage the situation. It also points to the need for and questions the "how to" build a corps of local media who are 'informed' about reporting research in an ethical manner

12. Community interest in dialogue vs Researcher's unwillingness to dialogue: Communities seemed willing to explore all the opportunities for dialogue (meetings, letters, visits) but researchers seemed unwilling to consider a second opinion. What could have informed such mannerisms? How do researchers view community? What is the true objective of community engagement in research for both parties? Is there a dedication on the part of researchers to promote mutual understanding between them and the community regarding research issues? While GPP represents a good start in dialogue, its adoption appears to be principally by community advocates.

13. Multi-country trials and information sharing: The report of this controversy also highlights the possible impact that the results and outcomes of a trial in one country can have on similar researches in other countries. the closure of the Nigeria's study and report of the Malawi government not granting ethical approval for the study may have been a key influence on decision making around the Cameroonian study.

Chapter 7:

Conclusion

Community engagement in research is recognized as important for the conduct of researches that are of public health significance. However, the focus of community engagement should not just be to facilitate community support so as to ensure a crisis free research, but to facilitate a process where the research goals are shared by the community and researcher. This would facilitate uptake and use of research outcomes long after the research is concluded.

The lessons learnt from the Tenofovir controversy continue to be applicable. Many second and third party accounts of the controversy have been reported. However, this first hand account of the incidence around the trial helps to facilitate community report and review of the incidence. The views shared in this report are examples of how some members of the affected communities perceived the cause of the controversy.

One can then insinuate from these written accounts and its analysis, when compared with the multiple journal publications on the issue, that community perspectives of the ethics of research somehow differ from the researcher perspectives: some of what the community oftentimes refer to as unethical are issues least considered for ethical deliberation by the researchers. Often times, the two communities use the same words; but then the words convey different meanings to either group. Is there a need to start a dialogue on the issue of 'ethical misrecognition' in clinical trials: a concept close to the notion of therapeutic misconception?

As highlighted in the analysis, there were some common themes that could be identified from all the reports. The authors however think that certain specific concerns are worthy of note especially at this time when multiple biomedical HIV prevention trials are being conducted within the same continents where these reported controversies occurred. One of such themes is the need to address provision of comprehensive care and treatment for trial participants.

Another important theme is the Good Participatory Practice (GPP) document that arose out of the ashes of the trials. The reports all acknowledged that this was a welcome tool for 'legalising' community advocates' voices over the issue of engaging communities as partners in research design and implementation: communities need to have a say in matters that affects them and their lives.

Also equally important, is that these narratives clearly show that no communities exist in isolation: just as researchers learn from each other in international events and through international contacts and e-communication, so too do communities and their advocates. Through this process, it is clear that communities are complex entities and no single process/structure will suffice for all.

This report raises a few questions in the mind of the authors - is there a need to review the interpretation of current ethical codes from the perspective of the community? What does community engagement in research truly mean? How much freedom does a community truly have to refuse the conduct of a trial in their community if they feel the community would not benefit from the research? What channels are there to truly address disputes between communities and other actors about the conduct of a research in a community? Who truly represents a community? How 'informed' is Informed Consent?

While this report does not try to answer these questions, it provides food for thought and raises issues which would continue to stimulate discussions among communities, researchers and relevant stakeholders engaged in the research at all levels. Hopefully, as NHVMAS continues its work in the field, it shall provide insights to community perspectives on some of these issues in subsequent monologue publications on the matter.

