



ALLIANCE FOR MICROBICIDE DEVELOPMENT

03 August 2007, Volume 8, Number 30

The Alliance for Microbicide Development *News Digest* is an **unedited** compilation of:

- Media coverage of microbicides;
- Abstracts of articles on microbicides and relevant science in peer-reviewed journals;
- Material on other reproductive health and HIV prevention technologies, including HIV vaccines; and
- Matters of policy and politics with importance for microbicide research, development, and advocacy.

Its purpose is to:

- Raise awareness around the range of opinions and information about microbicides disseminated in the press and scientific journals; and
- Provide a neutral, objective basis for decision-making and evidence-based advocacy.

The *News Digest* is produced in a web-based format. Readers can view complete issues of the Digest or search by keyword for individual articles at <http://www.microbicide.org/publications/>. If you would like to be removed from the *Digest* distribution list, please send an email to digest@microbicide.org. We welcome comments, questions, and ideas about other microbicide-relevant topics we might cover, services we might provide, and better ways of providing them!

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1. MONTHLY MICROBICIDE PIPELINE UPDATE

August 2007

<http://www.microbicide.org/microbicideinfo/reference/Microbicide.Ongoing.Clinical.Trials.Summary03Aug07.pdf>

Each month, the *Digest* includes an update on overall progress in the field. Currently, there are 11 **microbicide** candidates in clinical development and over 30 in preclinical development. As a continued effort to maintain the most up-to-date information, we urge you to visit the Alliance website at www.microbicide.org or contact Stephanie Tillman, Alliance Writer/Research Associate, by email (stillman@microbicide.org) or by phone (301-587-3302) with any updates, questions, or comments.

Please note: In the PDF version of the Digest, this table's formatting may render the entries difficult to interpret. For the correctly formatted version, please visit the web version of the Digest, or view the table on the Alliance's homepage at www.microbicide.org.

MICROBICIDE CANDIDATES IN ONGOING CLINICAL TRIALS: SUMMARY AS OF AUGUST 2007 *

<i>Phase</i>	<i>Candidate Name and Formulation</i>	<i>Mechanism of Action</i>	<i>Sites by Country</i>
3	Carraguard (R) gel	Entry-fusion inhibitor	South Africa
3	0.5% and 2% PRO 2000/5 gels	Entry-fusion inhibitor	South Africa, Tanzania, Uganda, Zambia
2B	1% Tenofovir gel ("CAPRISA 004")	Replication inhibitor	South Africa
2-2B	0.5% PRO 2000/5 gel (P) and BufferGel (R) ("HPTN 035")	Entry-fusion inhibitor and Vaginal defense enhancer	Malawi, South Africa, United States, Zambia, Zimbabwe
2	1% Tenofovir/PMPA gel	Replication inhibitor	India, United States
1-2	Dapivirine (TMC120) vaginal ring	Replication inhibitor	Belgium
1-2	Dapivirine (TMC120) gel	Replication inhibitor	Rwanda, South Africa, Tanzania
1-2	Invisible Condom (TM) gel	Entry-fusion inhibitor	Cameroon
1	Dapivirine (TMC120) vaginal ring	Replication inhibitor	Belgium
1	Dapivirine (TMC120) gel	Replication inhibitor	South Africa
1	1% Tenofovir/PMPA gel	Replication inhibitor	Dominican Republic, United States
1	0.1% UC-781 gel	Replication inhibitor	United States
1	0.1% and 0.25% UC-781 gel	Replication inhibitor	United States
1	0.1% and 0.25% UC-781 gel	Replication inhibitor	Thailand
1	3% VivaGel (TM) (SPL7013 gel)	Entry-fusion inhibitor	Puerto Rico, United States

1	3% VivaGel (TM) (SPL7013 gel)	Entry-fusion inhibitor	Kenya, United States
N-A	Vaginal ring safety and acceptability study	Placebo ring	Kenya, South Africa, Tanzania

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For modifications, please contact Stephanie Tillman, email stillman@microbicide.org, tel. +301-587-3302.

*AMD is in the process of modifying its reports on universal clinical trials of **microbicides** in all relevant formulations.

AMD These trials have completed and analysis of the final results is ongoing.

This device is intended for use with a **microbicide**.

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2. ALLIANCE UPDATES AND COMMUNITY NEWS

Alliance for Microbicide Development: Posters at IAS and ISSTD

The Alliance for **Microbicide** Development presented three posters at the International AIDS Conference (IAS) in Sydney and two posters at the International Society for STD Research (ISSTD) in Seattle. The titles of the posters are below. For more information on the posters, please email the Alliance at info@microbicide.org.

Posters presented at IAS:

- Trends and triggers: media and journal coverage of **microbicides** from 1992-2007
<http://www.iasociety.org/Default.aspx?pagelD=11&abstractId=200704635>
- The **microbicide** field response to clinical trial challenges
<http://www.iasociety.org/Default.aspx?pagelD=11&abstractId=200705159>
- Assays and models for **microbicide** research: the current inventory and possible implications
<http://www.iasociety.org/Default.aspx?pagelD=11&abstractId=200705067>

Posters presented at ISSTD: Monday, July 30: http://www.parthenon.com/eventure/welcome.do?type=public&congress=6_07STD

- Progress towards a **microbicide** for the prevention of sexually transmitted infections
- Topical **microbicides** and STIs: responses to clinical trial challenges

Deputy Director opening at the Alliance

<http://www.microbicide.org/allianceinfo/employment.shtml>

The Alliance for **Microbicide** Development is seeking a Deputy Director to join its team. The Deputy Director works with the Director to determine and develop the conceptual framework and to carry out key decision-making processes of the Alliance. This position requires the ability to work with minimal supervision. Relies on experience and judgment

to plan and accomplish goals. Requires superior communication and leadership skills. As a long-term goal, s/he could be considered for the role of Alliance Director.

Essential Duties:

- Works with Director on strategic planning/conceptual framework for the Alliance
- Works with Director on human resource and organizational development
- Works with Director to develop and apply evaluation techniques to assess, inform, and improve management decision-making processes, optimal staff productivity and satisfaction
- Leads/shares responsibility for financial systems oversight
- Responsible for Alliance Board recruitment, function and management
- Enhances engagement of donors
- Seeks new science with possible application to **microbicide** research and development
- Tracks policy issues surrounding the field
- Participates in staff representation at key conferences
- Supervises staff when Director is absent

Education/Experience:

- Masters degree + 10 years post-graduate experience or Doctoral degree in relevant discipline
- Background in science/research
- Experience in program management; nonprofit management; financial management
- Experience in, familiarity with, and commitment to public health, women's health, and/or HIV
- Experience working with Boards of Directors and Advisory Groups

Computer Skills:

- Proficiency in Microsoft Office 2003 and openness to new technologies

To apply, please email resume/CV and cover letter to Lois Holston at info@microbicide.org by 30 September 2007.

No phone calls or faxes please.

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3. MEDIA COVERAGE OF MICROBICIDES

"2 distinct diagnoses on world health"

Date: 31 July 2007

Source: *The Los Angeles Times*

Author(s): Ricardo Alonso-Zaldivar

<http://www.latimes.com/news/nationworld/politics/la-na-surgeon31jul31,1,6341268.story?ctrack=1&cset=true>

As then-Surgeon General Richard H. Carmona was preparing a report on world health problems, he received a detailed outline from officials at the Department of Health and Human Services. It suggested that he praise President Bush's initiative against AIDS in poor countries, and highlight American efforts to rebuild public health infrastructure in Iraq and Afghanistan. Instead, his report decried global pollution and violence against women. Carmona's 2006 draft described condoms as an effective way to prevent AIDS, omitted U.S. efforts on public health in Iraq and Afghanistan and made only passing references to Bush. The report was subsequently pigeon-holed and never released by the health department. The difference between the drafts, released Monday in Congress, added fuel to the controversy over whether the Bush administration has politicized science and medicine - putting political and ideological messages ahead of scientific information.

Carmona recently testified before Congress that his report was killed because it did not conform to administration doctrine, a charge the administration disputes. Health and Human Services spokesman Bill Hall said it was not released because a scientific review raised "strong concerns [from] multiple agencies" within the department, not because of politics. But Rep. Henry A. Waxman (D-Los Angeles), who Monday released both the departmental outline and Carmona's report, charged that the incident reflected the determination of Bush administration officials to politicize government agencies that were supposed to be insulated from partisan influence.

"Dr. Carmona's draft thoughtfully covers a wide range of global health topics," Waxman said in a letter to HHS demanding more information on the dispute. The department's draft, he said, "ignores or glosses over serious global health problems and emphasizes the achievements and policies of the Bush administration."

Carmona declined to comment on the controversy Monday, but said he would be ready to return to Congress and testify in greater detail, if asked. Other former surgeons general who testified alongside Carmona this month said political pressure had been a problem under Republican and Democratic administrations. They urged that Congress act to make the office of the surgeon general more independent.

The memo to Carmona was drafted by officials in an HHS office that deals with global health, headed by William R. Steiger, a political appointee first identified by the Washington Post as responsible for having bottled up the surgeon general's report. In an earlier statement, Steiger called Carmona's draft "a poorly written, general recitation of every disease problem in the world," adding that "the information it provided was often inaccurate or out-of-date, and it lacked analysis and focus."

Hall added Monday: "It was not just Bill Steiger and the office of global health - a number of other agencies - had strong concerns." The National Institutes of Health and the Food and Drug Administration were among the agencies that objected to the release of the report as presented by Carmona, he said.

Waxman said it was the information in the memo from Steiger's office that was inaccurate. For example, while omitting any mention that condom use can prevent AIDS infection, the HHS draft called attention to antimicrobial ointments "near final development" that women could use to protect themselves. Waxman called that misleading. "No **microbicide** has been approved for reducing HIV infection, and an international **microbicide** development organization predicts five to seven years until a product is available," Waxman said in his letter to HHS.

The two documents are posted on the Internet at oversight.house.gov.

Broadly speaking, Carmona's draft blames social problems such as poverty and man-made conditions such as pollution for much of the burden of disease in the world. The HHS memo tends to focus on pathogens, such as the H5N1 bird flu virus. Even on the ill effects of tobacco, a standard theme of public health reports, there are striking differences. Carmona's report mentioned tobacco 16 times, calling it the second major cause of death worldwide, and describing tobacco use as an "epidemic." The HHS memo only mentions it twice, acknowledging that reduced tobacco use promotes better health but hardly calling for a crusade.

Carmona said he wanted to issue a report on worldwide health, because in an era of globalization, health problems are no longer localized. "The hunger, disease and death resulting from poor food and nutrition create social and political instability in many nations, and that instability may spread to other nations as people migrate to survive," his draft report said. "Failing to address global health issues outside of our national border will only make problems much more challenging when they enter our country." Besides, he wrote, the U. S. could win friends and allies overseas by helping other countries confront their health problems.

"Remaining faithful a fine idea, but . . ."

Date: 29 July 2007

Source: *Sunday Tribune*

Author(s): Mike Seneka, Sabelo Zondo, Suzanne Leclerc-Madlala

<http://www.sundaytribune.co.za/>

Twenty-year-old Chris is a student at a Durban tertiary institution who works part-time as an HIV/Aids peer-educator for the institution's Student Counselling Centre. His job is to facilitate workshops that will spur fellow students to practice safe sex. When briefed about a recent UNAids report that identified a reduction in the number of concurrent sexual partnerships as possibly the key to reversing the tide of HIV/Aids in the region, his first reaction was to laugh. Then he added, "Now I know we are all going to die. That's what we don't want to do. That would be the end of life."

Equating life with the pursuit of love, and the excitement and intrigue of juggling several romantic relationships simultaneously, holds a particular irony for tens of thousands of young people like Chris living in Aids-ravaged Southern Africa. It's this very same pursuit that is resulting in an all-too-real "end of life". Discouraging casual sex outside marriage, and advocating mutual monogamy between sexual partners was once the special preserve of missionaries. Today, in the name of public health, as opposed to Christian morality, policy makers are being advised to do the same. But unlike efforts to promote HIV prevention through the use of condoms, **microbicides** or vaccines, the promotion of faithfulness is construed in much the same way as the promotion of abstinence; a nice idea but hardly realistic. Behavioural change in the context of HIV/Aids is possibly the most difficult and most contentious preventive measure to promote. Perhaps this explains why, as a society, we have long avoided this challenge. But, as with all things related to our tepid response to HIV/Aids, we have come to pay the price of shying away from the challenge.

While the "Be Faithful" element of the ABC approach to HIV prevention is only now being recognised as pivotal for averting further social and economic disaster in the region, this comes at a time when there seems to be greater

incentives for multiple sexual partnering than ever before. Studies on the views of tertiary-level students in Southern Africa - those who should know better according to some who still believe that HIV prevention is matter of awareness - reveal the challenge of convincing youngsters to forgo multiple concurrent partnering for the sake of disease prevention.

Whether studying marketing in Gaborone, education in Lusaka or psychology in Durban, students report that the stress of campus life and the pressures to keep up with, or impress peers, are major motivations for seeking and maintaining several sexual relationships simultaneously.

Girlfriends

For young men studying at regional tertiary institutions, the pressure to prove themselves as normal and manly in the eyes of their peers, is the number one reason given for their desire to have more than one girlfriend at a time. Keeping "back-ups", in the event that one disappoints you by cheating, is also given as a justification, as is the "problem" when a particular girlfriend is menstruating or doesn't want sex for whatever reason.

It is likely that the motivations for multiple partnering among men have not changed that much through time, unlike those for women. Women's motivations for seeking multiple partners appear to be more complex. For one thing, contemporary aspirations for gender equality often seem to carry a prescript for "doing as the men do". Tragically, those same aspirations are putting young women at very high risk for HIV.

For many young women students, being faithful to a singular boyfriend, whom they say is likely to already have other girlfriends or, if not, will at some point get others, is viewed as senseless, and some would even say stupid. Additional boyfriends act as a hedge against heartbreak, providing a ready shoulder to cry on in the expected eventuality that one boyfriend will hurt you. In the words of Gladys from Zambia, "Having several partners is to me an advantage because when one disappoints you, another comforts you. It reduces your stress. When I hear so-and-so is cheating, I just don't worry as I'm doing the same. You can never trust men".

University women in Botswana hold similar views, "It's rather stupid to be faithful to one as he'll betray you. Then you feel unattractive and uncared-for, even suicidal, so what's the use?" For many women students in Southern Africa, having multiple concurrent partnerships contributes towards boosting self-esteem and feeling loved.

Beyond psychological and emotional reasons for maintaining a small stable of boyfriends, there are financial and social reasons. It is largely for these reasons that older boyfriends are entertained; they have jobs and social standing in the communities. Young women students view their liaisons with older men as "networking".

While they may not admit to it when filling out a survey questionnaire, many, if not most young people in the region, know they are at risk of contracting HIV. Increased knowledge of HIV/Aids seems to have led to a tacit acceptance of HIV risk, and it's a risk they are willing to take. For people like Chris, who are tasked with convincing their peers to take the threat of HIV/Aids more seriously, peers who associate sticking to one partner with the "end of life", promoting faithfulness means nothing less than attempting a re-orientation in what is for many a way of life.

As difficult as it may be, our best hope for a long-term solution to the HIV/Aids crisis lies in changing that very way of life.

4. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

"In vitro pre- and post-exposure prophylaxis using HIV inhibitors as microbicides against cell-free or cell-associated HIV-1 infection"

Author(s): Terrazas-Aranda K, Van Herrewege Y, Lewi PJ, et al

Reference: N/A 18(3):141-51. In process.

http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&dopt=AbstractPlus&list_uids=17626598

Published Abstract: Several classes of **microbicides** are being evaluated for the prevention of sexual HIV transmission. In vivo, the infectious dose and viral source involved in transmission remain uncertain and it is likely that women will use **microbicides** both before and after high-risk HIV exposure. Therefore, we evaluated HIV entry inhibitors (EIs) and reverse transcriptase inhibitors (RTIs) for their ability to block cell-free and cell-associated HIV-1 infection in co-cultures of monocyte-derived dendritic cells (MO-DC) and CD4+ T-cells using settings of pre- and post-exposure prophylaxis. In the pre-exposure assay, where compound was present before, during and 24 h after infection, all tested EIs (BMS806, TAK779 and T20) and RTIs (PMPA, TMC120 and UC781) blocked infection with 10(-4) multiplicity of infection (MOI) of cell-free virus at a dose between 100 and 10,000 nM, dependent on the compound used. At 10(-3) MOI, however, only T20 and the RTIs completely blocked infection. Furthermore, in experiments with cell-associated virus, EIs were ineffective, whereas RTIs actively blocked infection with similar potency as in the experiments with cell-free virus. In the post-exposure assay, where compound was added 2 h after infection and remained present for 24 h, EIs were inactive whereas RTIs blocked cell-free and cell-associated viral infections equally efficiently. Moreover, post-exposure prophylaxis initiated 24 h after infection with cell-free or cell-associated HIV-1 was still effective with 1,000 nM of TMC120. Both EIs and RTIs were non-cytotoxic at any tested concentration for MO-DC and CD4+ T-cells in co-culture. Our study shows that RTIs are potent inhibitors of cell-free and cell-associated virus used either in pre- or post-exposure settings. It highlights that parameters such as viral input, viral source, the time of compound addition and the target cells should be considered in **microbicides** evaluation.

"South Africa's experience of the closure of the cellulose sulphate microbicide trial"

Source: *PLoS Med.* 2007 Jul 31;4(7):e235.

Author(s): Gita Ramjee, Roshini Govinden, Neetha S Morar, et al

<http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0040235>

In sub-Saharan Africa, almost 60% of HIV infections are among women [1], and the number of new HIV infections in women worldwide continues to escalate. The high incidence of HIV in many African countries provides the optimum environment for research on technologies that could prevent women from becoming infected, including **microbicides**. In this article, we discuss the recent highly publicised closure of a trial of cellulose sulphate (CS), which we conducted. We discuss the impact of the closure on the participants, the community at the trial site and the public at large, the public health sector, national regulatory bodies, the media, and on other ongoing **microbicide** trials. The local lessons that we learnt from the closure may provide guiding principles for researchers and advocates in the HIV prevention field as a whole, who may face similar situations in the future.

*Previous **Microbicide** Trials*

Vaginal **microbicides** are products which, when applied to the vagina, may prevent HIV transmission. Such a product would be particularly valuable for women who are unable to negotiate condom use with their partners, since its use would be initiated by the woman. The concept of a vaginal **microbicide** was tested several years ago using an over-the-counter spermicide, nonoxynol-9, a surfactant that acts by disrupting cell membranes. The trial, conducted in several African countries, showed an increase in risk of HIV among women who used the product more than three times a day [2].

The trial outcome was a huge setback for the **microbicide** field. Nevertheless, almost a decade later, there are several products in large-scale clinical trials. These products were developed as a result of a better understanding of HIV-1 pathogenesis, including identification of HIV target cells [3].

In 2006, there was another disappointment with the stoppage of two trials of C31G (known as SAVVY), an antimicrobial and spermicidal agent. The trials were stopped because the HIV incidence was lower than expected in the target population, and it was unlikely that the trials would be able to show efficacy against HIV [4]. There were no safety concerns with the product.

Of the current products in large-scale effectiveness trials, almost all belong to a class of compounds called fusion inhibitors. These act by preventing the virus from attaching to the target cells in the vagina. The current generation of products has poor specificity to HIV. Two have contraceptive properties, three (BufferGel, Carraguard, and PRO 2000) have displayed in vitro evidence of inhibition of other sexually transmitted infections, and all of them are coitally dependent - that is, they must be used just prior to sexual intercourse [5].

Until recently there were five products in large-scale phase IIb/III trials [6]: cellulose sulphate (Polydex Pharmaceuticals; <http://www.polydex.com/>) [7-11], PRO 2000 0.5% and 2% (Indevus Pharmaceuticals; <http://www.indevus.com/>) [12], Carraguard (Population Council; <http://www.popcouncil.org/>) [13,14], and BufferGel (ReProtect; <http://www.reprotect.com/>) [15]. Clinical trials of BufferGel and PRO 2000 are still ongoing in several parts of Africa (Figure 1). A clinical trial of Carraguard was completed in March 2007, and data analysis is in process. All ongoing clinical trials are reviewed regularly for safety by an external committee of experts-the data safety and monitoring committee (DSMC).

Closure of the CS Trial

In early 2007, there was another huge disappointment. The randomised controlled trial testing 6% cellulose

sulphate against a placebo gel for effectiveness against vaginal transmission of HIV, sponsored by the reproductive health research organisation CONRAD (<http://www.conrad.org/>), was stopped following recommendations by the DSMC after preliminary data review of 1,333 enrolled women from five sites (South Africa, Uganda, Benin, and two sites in India) suggested that there were more HIV seroconversions in the cellulose sulphate arm compared to the placebo arm of the trial. This unexpected outcome was a huge blow to the **microbicide** field as CS, a non-cyclic antimicrobial agent, had been tested in several safety trials previously and there were no concerns about safety based on these trials [16].

The study DMSC was requested to provide guidance to the investigators if data indicated a difference of $p < 0.10$ for futility or harm. At the first review of 1,333 women in late January 2007, there were 35 seroconversions from the three African sites, with a higher number of HIV seroconversions in the CS arm compared to the placebo arm. The interim data analysis suggested that the boundary for safety had been crossed, and so the DMSC recommended stopping the trial to ensure the safety of the participants [17]. Data analysis is still ongoing to ascertain the reasons why the product was found to be potentially harmful. Another trial of the same product at two sites in Nigeria did not show the same effect but was also stopped as a precautionary measure for the participants' safety [18].

Investigators at all sites were informed by CONRAD on 29 January 2007 of the trial closure and a press release was planned for 31 January 2007 [12]. The key message of the press release was that the trial was stopped because it was found that CS could lead to an increased risk of HIV.

Actions, Challenges, and Responses to the Trial Closure

The HIV Prevention Research Unit (HPRU) of the Medical Research Council (MRC) in South Africa participates in all ongoing **microbicide** trials. Prior to the release of the press statement by CONRAD, we immediately developed a communication strategy to ensure that the information to stakeholders came from the local researchers (Table 1 and 2). Two days before the press release, we sent letters to the national and provincial departments of health, to the Medicines Control Council, which is South Africa's drug regulatory authority, and to the ethics committee that had approved the trial, informing them of the trial closure with a request for an urgent meeting.

We also sent letters to all community partners advising them that there were new developments in **microbicide** research, and requested community meetings at local levels. These letters did not provide details of the outcome of the trial as we felt it was better to give these details in a larger community meeting. We made contact with non-governmental organisations, advocacy groups (such as the Gender AIDS Forum; see <http://www.gaf.org.za/>), women's groups, and, most importantly, the research participants of the CS trial itself (Table 1 and 2). Community outreach staff encouraged all participants to use the toll-free telephone numbers set up at all HPRU research sites for any questions and concerns. The **vaginal gel** (CS or placebo) was collected within one week from 80% of the women in the trial. Currently, 95% of the women have been successfully notified.

We contacted a journalist who writes regularly about HIV/AIDS issues, and asked her to write an article in a local newspaper providing information on the trial and reasons for its closure to avoid potential sensationalist reporting.

Negative Press

Despite these proactive steps to inform the wider community, some reporters wrote inaccurate and sensational stories. For example, on 4 February 2007, a national weekly newspaper ran stories with the headlines "Medical research trial guinea pigs contract HIV" [19] and "Study to prevent AIDS left me infected". These reports included sensational statements such as "Hundreds of women in South Africa, Benin, Nigeria, Uganda and India, who are being used as human guinea pigs in the US-funded research on HIV prevention, are feared to have contracted the virus during the course of the trials" [19]. In fact there were 35 sero-incident cases among 1,333 participants across all the African trial sites. This alarmist statement instilled fear amongst all trial participants. Statements in the article saying, for example, that women felt "used and misled" [19] falsely implied that the conduct of the study was unethical.

Subsequently, these sensational articles led to many spin-off articles in other local and national papers, including local language newspapers (Table 3). News stations were confused by the messages in these articles, and we were interviewed by several radio and television stations in order to clarify the concerns.

The national Department of Health (DOH) requested a meeting with us to discuss the trial closure. Following this meeting, the minister of health, in consultation with her advisory committee, issued a press statement with the key message that all **microbicide** trials in South Africa would be investigated for ethical conduct [20]. This was the correct stance to take given the volatile situation, and we welcomed investigation of the trial conduct [21]. However, we believe it would have been an ideal opportunity to inform the larger population of the stringent and world-class ethical and regulatory standards that govern South African clinical trials. We believe that the DOH could have given a more balanced view of the situation. Such a view would have acknowledged that:

(1) the DOH is well informed of all clinical trials undertaken in the country through its clinical trial registry; (2) South Africa has national good clinical practice guidelines that must be followed for clinical trials; (3) all **microbicide** trials were conducted after thorough review of the protocols by ethics committees and drug regulatory authorities, with the latter governed by the DOH; and (4) these trials are regularly monitored by external reviewers.

Similar meetings on trial conduct were held with the local KwaZulu-Natal DOH and the Parliamentary Health Portfolio Committee, a parliamentary subcommittee of members of parliament tasked to address health issues.

*Impact upon Ongoing **Microbicide** Trials*

Given that HPRU is involved in many clinical trials, the challenge was not only to address the closure of the CS trial, but to address the concerns of communities at trial sites of other ongoing **microbicide** trials in KwaZulu-Natal.

We had several meetings with political ward councillors, research communities, and other concerned stakeholders (Table 2). Communities misinterpreted the minister of health's press release, wrongly believing that the minister had called for all gel (**microbicide**) trials to be stopped (she had not-she had launched an investigation of the conduct of all **microbicide** trials). There were many irate people demanding answers to the following questions: (1) "Is it not unethical for researchers to ask innocent

women to sleep with HIV-positive men so that we can test to see if the gel works?"; 2) "Is it true that gel increased the risk of HIV infection among innocent women?"; 3) "Why did researchers expose poor black women to the infected gel?"; and 4) "How did researchers explain the study to illiterate women?"

Clinical trial investigators in South Africa are required by the Medicines Control Council to reimburse trial participants with a minimum of R150 for trial participation to cover time, travel, and refreshments. But the general public's perception was that women were "bought to sleep with HIV-positive men". Many people believed that the gel contained HIV or that simply inserting the gel increased the risk of HIV infection irrespective of the sexual act. Responses from trial participants such as "you infected us with HIV" gave credence to these misconceptions. Although the community entry, approval, and educational process of clinical trials was thorough at the start of all trials, there was confusion as many communities doubted the information given to them at the outset prior to trial implementation. Furthermore, some people expressed concern about the racial demographics of the trial participants, believing that we had "targeted" rural, poor, uneducated, and vulnerable women. The CS trial was in fact conducted at an urban site in Durban.

Impact on Study Participants

Participants from all other **microbicide** trials were affected by closure of the CS trial. Male partners who knew about women's participation in other trials raised concerns that using "gel" increased HIV risk and did not want their female partners to participate in the trial. However, most women eventually decided to continue once they and their partners were counselled.

Peer educators in the community, who are also trial participants, were angry that the media described them as "poor", "vulnerable", "uneducated", and "guinea pigs". Women requested the researchers to link them to the media and the journalists who published inaccurate information so that they could voice their concerns. Most of the CS trial participants did not feel that trial participation increased their risk for HIV infection. They valued the benefit of being in the study. Less than ten of the CS trial participants believed the information in the press articles and were understandably upset. All except two participants agreed to speak and listen to staff, who allayed participants' fears. Two irate participants came to the clinic to return their gel and accused the researchers of trying to infect them with HIV. The partner of one participant burnt her gel supplies. Three participants and their partners attended the clinic for counselling.

Recommendations for Communicating about HIV Prevention Trials

- Emphasise community education.
- Explain and emphasise to the community that HIV seroconversion is the only way to measure effectiveness of new prevention technologies including **microbicides** (i.e., there are no surrogate markers of infection that can be used in trials).
- Educate the media and community about clinical trials, including regulatory procedures and good clinical practice guidelines followed by clinical trialists.
- Develop early drafts of press releases of all possible DSMC outcomes-positive, negative, and no effect-in partnership with local researchers and community representatives.
- Inform local ethics committees, drug regulatory authorities, and health authorities of trial outcome prior to press release.

- In drafting press releases, be sure to include the contribution of in-country investigators, community advisory boards, and other relevant bodies.
- Issue the press release in developing countries where the research is conducted. At the press conference, it is valuable to include the local principal investigator and representatives of the trial sponsor, ethics committee, and the local health authority.

Lessons Learnt

The outcome of the nonoxynol-9 trial in 2000 was a huge setback for **microbicide** research in South Africa. Health authorities, ethics committees, and drug regulators were concerned about the safety of **microbicide**s. Although the nonoxynol-9 trial received negative press, it was not as damaging at the community level as the closure of the CS trial, perhaps due to higher awareness now of **microbicide** clinical trials in South Africa as a whole. Furthermore, the 2006 closure of the SAVVY trial did not have an impact on current trials, possibly because the closure was not safety-related.

We learned several lessons from the closure of the CS trial that will provide us with a better understanding of communication strategies that may be required in many developing countries to deal with such situations in the future if they arise. Our recommendations for communicating about HIV prevention trials are shown in Box 1.

The first lesson we learned is that the phrasing of the CONRAD press release was open for misinterpretation by the lay public. Due to regulatory requirements of publicly traded companies such as Polydex Pharmaceuticals, which developed the CS **microbicide**, it was impossible for CONRAD to ensure that all sites were included in drafting the press release. We suggest that sponsors and in-country investigators be proactive and prepare communication strategies based on all possible outcomes of DSMC reviews whether they be positive, negative, or no effect. We also recommend that these potential messages be developed in consultation with local researchers, community advisory boards, or community representatives. Such advice from the community on shaping messages would help to reduce the risk of facts being distorted, and would help deliver the messages in a manner which is appropriate to the community's knowledge and understanding.

It is important that local health regulators such as the department of health and other governing bodies be kept informed on every aspect of the trial. Although regular updates were sent to the department, the frequency of updates was clearly not sufficient especially regarding negative outcomes of clinical trials. Quarterly meetings would ensure that the department is kept informed of all aspects of ongoing clinical trials. It is imperative that trial outcomes are reported to the department by local investigators prior to media release.

Similarly, the ethical review of clinical trials needs to be strengthened. Currently regulatory bodies approve clinical trials, but site reviews on the conduct of trials are limited, primarily due to lack of human capacity. It is important to boost the capacity of local ethics committees and other regulatory bodies to ensure that once the trials are approved, the sites are reviewed regularly so that there are no doubts created about trial conduct when there are unexpected trial outcomes.

For principal investigators (PIs), our experience provides a valuable lesson on the importance of ensuring involvement of communities in all aspects of research, including disseminating messages about clinical trial outcomes. Communities and participants should be kept updated on not only the trial in their community, but on outcomes of trials of other prevention technologies. Such open and transparent communication will improve the community's confidence in the researchers.

Fact sheets for communities need to be developed urgently once outcomes of prevention technologies are known. We have learnt that in addition to informing participant communities of the trial conducted in their community, it is important for us to provide them with an understanding of clinical trials in general. They need to understand that new drugs and interventions can only be introduced if the country's regulatory authority is convinced by the evidence of the quality, safety, and efficacy of the new product, and that such evidence can only come from clinical trials. They need to understand that clinical trials are particularly important if the product is designed for use by healthy individuals over a prolonged period of time, and that trials should preferably be conducted in communities that will use the product in case there are unforeseen pharmacogenetic interactions.

Perhaps the most important lesson learnt was that there is a need to educate the media on clinical trials as well as on the regulatory procedures and good clinical practice guidelines followed by clinical trialists. Despite our attempts to ensure that correct facts were published, the public was more attracted by sensational press articles. In most cases the media are hungry for news that will make headlines irrespective of whether the news is accurate or not. We suggest that sponsors and researchers set up media education sessions for each of the trials prior to implementation but also prior to results being released so that journalists have a good understanding of the outcomes of clinical trials and interpretation of data.

Since it is likely that most HIV prevention efficacy trials will be conducted in developing countries with high HIV incidence, we believe that the first press conference on a trial's results should be held in participating countries with the presence of the national principal investigator, a representative of the study's sponsor, and representatives from the local department of health and ethics committee. The in-country media would have the opportunity to direct any questions, concerns, or points of clarification to the principal investigator and sponsor rather than interpreting the results themselves. In our consultations with key journalists in Durban after the closure of the CS trial, they expressed the need to receive regular updates on **microbicides** and prevention research, rather than only receiving "bad" news about these trials.

One of the major challenges in HIV prevention research is that there are no surrogate markers for efficacy. The only way to assess effectiveness of products is to measure new HIV infections as an outcome. It thus becomes extremely difficult to make the lay public understand that in all prevention trials, participants are likely to become infected irrespective of the intervention, and it is not the researcher's aim to increase infection or risk of infection. Prevention packages are provided to avoid infection, including safe sex counselling, provision of male and female condoms, treatment of sexually transmitted infections, and intense scrutiny of safety markers such as ulceration and abrasions in vaginal **microbicide** trials in particular. Although such packages may reduce HIV incidence overall, it is our ethical imperative to provide as much preventive advice as possible to reduce the rate of new HIV infections. One of the lessons here is to make the broader community understand more clearly that the only way we can test effectiveness of an

HIV prevention technology is to assess the number of new HIV infections.

Conclusion

The closure of the CS trial has underscored the challenges we may face in the event of early trial closure due to a negative outcome. We now have insights on how to prepare for outcomes of future HIV prevention technologies and, at a minimum, prepare strategies to ensure that the messaging and process of message delivery is developed with local investigators, participant communities, local regulatory authorities, and in-country media.

We believe that the lessons learnt here will provide guidance to the HIV prevention field as a whole, as negative trial outcomes affect the future of HIV prevention research in the developing world.

Acknowledgments

We would like to thank Sicelo Gumede and the HPRU community liaison officers, field staff, and clinic staff who worked tirelessly three weeks post-closure to ensure that all communities and all trial participants were contacted and well informed. We thank the DOH, both National and Provincial, as well as the Parliamentary Health Portfolio Committee for giving us an opportunity to clarify and provide further information on CS and other **microbicide** trials. Our sincere thanks to the communities, community leaders, and community advisory members who took time off to listen to us and also to be frank and honest about their concerns. We thank Lut Van Damme from CONRAD for being present for a couple of the meetings held with stakeholders. We thank Melanie Mills for her administrative and communication support throughout this difficult time. We thank Prof. Janet Darbyshire for her very thoughtful comments. We thank all our sponsors and partners for their ongoing support and assistance. Last but not least, our heartfelt thanks go to our research participants for their trust and support despite all the negativity we experienced.

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"The utility of non-proportional quota sampling for recruiting at-risk women for microbicide research"

Author(s): Morrow KM, Vargas S, Rosen RK, et al

Reference: N/A 11(4):586-95.

<http://www.springerlink.com/content/v5268t2h61l354t1/>

Published Abstract: In the context of a measurement development study designed to contextualize **microbicide** acceptability, a sample that represented a range of at-risk women and maintained the statistical power needed for validity analyses was required. A non-proportional quota sampling strategy focused on race/ethnicity and number of sexual partners was utilized. This strategy resulted in enrollment of approximately equal proportions of Latina (31%), Black (36%), and White (32%) women, and an approximately 1:2 ratio of single-partnered (29%) and multi-partnered (71%) women. About 17% of women screened were ineligible based on eligibility criteria; an additional 16% were ineligible based on quota closures. Most participants were recruited through word of mouth (39%), community-based organizations (19%), or media sources (19%). Women recruited through word of mouth had the highest screen-to-interview completion percentage (67%). Non-proportional quota sampling is a feasible option for ensuring adequate representation of sample characteristics in **microbicide** research, but this goal should be weighed against cost and staff burden.

"Validity of coital diaries in a feasibility study for the Microbicides Development Programme trial among women at high risk of HIV/AIDS in Mwanza, Tanzania"

Author(s): Allen CF, Lees SS, Desmond NA, et al

Reference: N/A Epub ahead of print.

<http://sti.bmj.com/cgi/content/abstract/sti.2007.024810v1?ct=ct>

Published Abstract: *Objectives:* To compare coital diaries (CDs) and face-to-face interviews (FFIs) in measuring sexual behaviour among women at high risk of HIV To assess the effect of differing levels of support from researchers on reporting in CDs and FFIs. *Methods:* Three groups of 50 women were randomly selected from a cohort of food and recreational facility workers participating in a **microbicide** trial feasibility study and received differing levels of researcher support. Minimum support involved delivering and collecting CDs weekly; medium support included a weekly FFI and discussion of concerns; intensive support also included an unscheduled mid-week visit when diaries were checked and concerns addressed. All respondents participated in an exit FFI, including questions on sexual

behaviour over the four-week study period and study acceptability. *Results:* Sexual behaviours were generally reported more frequently in CDs than weekly or exit interviews. Vaginal and anal sex, male and female condom use, vaginal cleaning and lubrication, sex during menstruation and sex with irregular and regular partners were reported more frequently in CDs than exit interviews. In CDs, level of support was associated with reporting of vaginal sex and cleaning. In exit interviews, support level was associated with reporting of vaginal sex, vaginal cleaning and sex with regular, irregular and commercial partners. Women with minimum support reported least satisfaction with the research process. Women with intensive support were most likely to report that they informed someone about their study participation and that they completed diaries daily. *Conclusions:* Compared with FFIs, CDs resulted in higher reporting of socially stigmatised activities, and sexual behaviour reporting varied less by level of support. More researcher support enhanced study acceptability.

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5. PUBLISHED RESEARCH: RELEVANT BASIC AND TRANSLATIONAL SCIENCE

"Design of helical, oligomeric HIV-1 fusion inhibitor peptides with potent activity against enfuvirtide-resistant virus"

Author(s): Dwyer JJ, Wilson KL, Davison DK, et al

Reference: N/A 104(31):12772-77.

<http://www.pnas.org/cgi/content/abstract/104/31/12772?etoc>

Published Abstract: Enfuvirtide (ENF), the first approved fusion inhibitor (FI) for HIV, is a 36-aa peptide that acts by binding to the heptad repeat 1 (HR1) region of gp41 and preventing the interaction of the HR1 and HR2 domains, which is required for virus-cell fusion. Treatment-acquired resistance to ENF highlights the need to create FI therapeutics with activity against ENF-resistant viruses and improved durability. Using rational design, we have made a series of oligomeric HR2 peptides with increased helical structure and with exceptionally high HR1/HR2 bundle stability. The engineered peptides are found to be as much as 3,600-fold more active than ENF against viruses that are resistant to the HR2 peptides ENF, T-1249, or T-651. Passaging experiments using one of these peptides could not generate virus with decreased sensitivity, even after more than 70 days in culture, suggesting superior durability as compared with ENF. In addition, the pharmacokinetic properties of the engineered peptides were improved up to 100-fold. The potent antiviral activity against resistant viruses, the difficulty in generating resistant virus, and the extended half-life in vivo make this class of fusion inhibitor peptide attractive for further development.

"Endoribonuclease-prepared siRNAs induce effective and specific inhibition of HIV-1 replication"

Author(s): Gimenez-Barcons M, Clotet B, Martinez MA

Reference: N/A Epub ahead of print.

http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=17652404&dopt=AbstractPlus

Published Abstract: Short interfering RNAs (siRNAs) targeting viral or cellular genes can efficiently inhibit human immunodeficiency virus type 1 (HIV-1) replication. Nevertheless, optimal HIV-1 gene silencing by siRNA requires precise complementarity with most of the target sequence. The emergence of mutations in the targeted gene could lead to rapid viral escape from the siRNA. In the present study, *Escherichia coli* endoribonuclease III (RNase III) or mammalian Dicer was used to cleave double-stranded RNA into endoribonuclease-prepared siRNA (esiRNA). EsiRNAs generate a variety of siRNAs, which can efficiently and specifically target multiple sites in the cognate RNA. EsiRNAs targeting the region encoding the HIV-1 reverse transcriptase (RT) reduced viral replication by 90%. The inhibition was dose-dependent and sequence-specific because several irrelevant esiRNAs did not inhibit HIV-1 replication. Importantly, esiRNAs obtained from the prototypic RT sequence of the HXB2 strain and from highly mutated RT sequences showed a similar degree of viral inhibition, suggesting that the heterogeneous population of esiRNAs could overcome individual mismatches in the RT sequence. Finally, esiRNAs generated by Dicer cleavage were five times more potent than those generated by bacterial RNase III digestion. These results show that esiRNAs are potent HIV-1 inhibitors. Moreover, sequence targets do not need to be highly conserved to reach a high level of viral replication inhibition.

"Identification and characterization of UK-201844, a novel inhibitor that interferes with HIV-1 gp160 processing"

Author(s): Blair WS, Cao J, Jackson L, et al

Reference: N/A Epub ahead of print.

http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=17646410&dopt=AbstractPlus

Published Abstract: Greater than 10(6) compounds were evaluated in an HIV-1 high throughput antiviral screen resulting in the identification of a novel HIV-1 inhibitor (UK-201844). UK-201844 exhibited antiviral activity against HIV-1 NL4-3 in MT-2 and PM1 cells with EC50 values of 1.3 and 2.7 microM, respectively, but did not exhibit measurable antiviral activity against the closely related HIV-1 IIB lab strain. UK-201844 specifically inhibited the production of infectious virions packaged with an HIV-1 envelope (Env) but not HIV virions packaged with a heterologous Env (i.e., the vesicular stomatitis virus glycoprotein), suggesting that the compound targets HIV-1 Env late in infection. Subsequent antiviral assays using HIV-1 NL4-3/IIB chimeric viruses showed that HIV-1 Env sequences were critical determinants of UK-201844 susceptibility. Consistent with this, in vitro resistant virus studies revealed that amino acid substitutions in HIV-1 Env are sufficient to confer resistance to UK-201844. Western analysis of HIV Env proteins expressed in transfected cells or in isolated virions showed that UK-201844 inhibited HIV-1 gp160 processing resulting in the production of virions with non-functional Env glycoproteins. Our results demonstrate that UK-201844 represents the prototype for a unique HIV-1 inhibitor class that directly or indirectly interferes with HIV-1 gp160 processing.

6. HIV/AIDS VACCINES

"Scientist gets \$15 Million grant to develop potential AIDS vaccine"

Date: 01 August 2007

Source: *The Washington Post*

Author(s): Lisa Rein

<http://www.washingtonpost.com/wp-dyn/content/article/2007/07/31/AR2007073101559.html?wpisrc=newsletter>

The University of Maryland scientist who co-discovered the virus that causes AIDS is receiving a \$15 million grant from the Bill and Melinda Gates Foundation to develop a potential vaccine, state officials announced yesterday. Dr. Robert Gallo said he expects the five-year grant to expand his research on a possible vaccine that he has tested successfully on monkeys.

"We have a vaccine candidate that we think is extremely interesting and unique in its properties," Gallo said yesterday at a news conference in Annapolis. Gallo, director of the Institute of Human Virology at the University of Maryland's School of Medicine, said he hopes to begin clinical trials next year.

Gallo and French researcher Luc Montagnier were the first to identify that the human immunodeficiency virus causes AIDS. But more than two decades after the epidemic began, the search for a vaccine continues, presenting one of the toughest challenges in medicine.

HIV mutates rapidly and integrates into a patient's genetic material, making it a moving target that infects the immune cells the body uses to fight an attack. Dozens of trials are underway, but attempts to develop a vaccine have failed because researchers have not been able to stop the strains of the virus from reappearing. Drugs in an infected person's bloodstream can kill the virus, but they can't touch it in the body's immune cells. More than 25 million people have died of AIDS since 1981, and about 40 million are living with HIV, most of them in Africa. Yesterday, Gallo compared the death toll from AIDS to the toll from the tsunami that crashed onto an Indonesian island in 2005.

"Two hundred thousand people died in the tsunami," he said. "Every month, 250,000 people die of AIDS."

The grant, announced by Gov. Martin O'Malley (D), is part of the Gates Foundation's Collaboration for AIDS Vaccine Discovery, an international network of researchers hunting for a vaccine. The effort started last year with \$287 million in grants.

Gallo said he has been working in earnest on a potential vaccine for about four years. The approach of his team of researchers is to intercept the virus before it can enter the body's cells and attack the immune system's response to an infection. That would give the antibodies the best chance of working against the various strains of HIV, he said. He also said the vaccine has the potential to eliminate the virus in already infected cells.

Gallo has a public-private partnership with Wyeth Pharmaceuticals and Profectus BioSciences, a spinoff of the Institute of Human Virology, which would help fund clinical trials and manufacture the vaccine.

7. POLITICS AND POLICY

"Why Africa fears Western medicine"

Date: 31 July 2007

Source: *The New York Times (Op-Ed)*

Author(s): Harriet A Washington

<http://www.nytimes.com/2007/07/31/opinion/31washington.html?ex=1186545600&en=414793185d54fca2&ei=5070&emc=eta1>

EDITOR'S NOTE: *This article by Harriet Washington, and the one following it in this Digest, by Jonny Steinberg, are both included because they present two different perspectives on the issue, and both are illuminating and merit our attention.*

To Westerners, the repatriation of five nurses and a doctor to Bulgaria last week after more than eight years' imprisonment meant the end of an unsettling ordeal. The medical workers, who in May 2004 were sentenced to death on charges of intentionally infecting hundreds of Libyan children with H.I.V., have been freed, and another international incident is averted.

But to many Africans, the accusations, which have been validated by a guilty verdict and a promise to reimburse the families of the infected children with a \$426 million payout, seem perfectly plausible. The medical workers' release appears to be the latest episode in a health care nightmare in which white and Western-trained doctors and nurses have harmed Africans - and have gone unpunished.

The evidence against the Bulgarian medical team, like H.I.V.-contaminated vials discovered in their apartments, has seemed to Westerners preposterous. But to dismiss the Libyan accusations of medical malfeasance out of hand means losing an opportunity to understand why a dangerous suspicion of medicine is so widespread in Africa.

Africa has harbored a number of high-profile Western medical miscreants who have intentionally administered deadly agents under the guise of providing health care or conducting research. In March 2000, Werner Bezwoda, a cancer researcher at South Africa's Witwatersrand University, was fired after conducting medical experiments involving very high doses of chemotherapy on black breast-cancer patients, possibly without their knowledge or consent. In Zimbabwe, in 1995, Richard McGown, a Scottish anesthesiologist, was accused of five murders and convicted in the deaths of two infant patients whom he injected with lethal doses of morphine. And Dr. Michael Swango, ultimately convicted of murder after pleading guilty to killing three American patients with lethal injections of potassium, is suspected of causing the deaths of 60 other people, many of them in Zimbabwe and Zambia during the 1980s and '90s. (Dr. Swango was never tried on the African charges.)

These medical killers are well known throughout Africa, but the most notorious is Wouter Basson, a former head of Project Coast, South Africa's chemical and biological weapons unit under apartheid. Dr. Basson was charged with killing hundreds of blacks in South Africa and Namibia, from 1979 to 1987, many via injected poisons. He was never convicted in South African courts, even though his lieutenants testified in detail and with consistency about the

medical crimes they conducted against blacks.

Such well-publicized events have spread a fear of medicine throughout Africa, even in countries where Western doctors have not practiced in significant numbers. It is a fear the continent can ill afford when medical care is already hard to come by. Only 1.3 percent of the world's health workers practice in sub-Saharan Africa, although the region harbors fully 25 percent of the world's disease. A minimum of 2.5 health workers is needed for every 1,000 people, according to standards set by the United Nations, but only six African countries have this many.

The distrust of Western medical workers has had direct consequences. Since 2003, for example, polio has been on the rise in Nigeria, Chad and Burkina Faso because many people avoid vaccinations, believing that the vaccines are contaminated with H.I.V. or are actually sterilization agents in disguise. This would sound incredible were it not that scientists working for Dr. Basson's Project Coast reported that one of their chief goals was to find ways to selectively and secretly sterilize Africans.

Such tragedies highlight the challenges facing even the most idealistic medical workers, who can find themselves working under unhygienic conditions that threaten patients' welfare. Well-meaning Western caregivers must sometimes use incompletely cleaned or unsterilized needles, simply because nothing else is available. These needles can and do spread infectious agents like H.I.V. - proving that Western medical practices need not be intentional to be deadly.

Although the World Health Organization maintains that the reuse of syringes without sterilization accounts for only 2.5 percent of new H.I.V. infections in Africa, a 2003 study in *The International Journal of S.T.D. and AIDS* found that as many as 40 percent of H.I.V. infections in Africa are caused by contaminated needles during medical treatment. Even the conservative W.H.O. estimate translates to tens of thousands of cases.

Several esteemed science journals, including *Nature*, have suggested that the Libyan children were infected in just this manner, through the re-use of incompletely cleaned medical instruments, long before the Bulgarian nurses arrived in Libya. If this is the case, then the Libyan accusations of iatrogenic, or healer-transmitted, infection are true. The acts may not have been intentional, but given the history of Western medicine in Africa, accusations that they were done consciously are far from paranoid.

Certainly, the vast majority of beneficent Western medical workers in Africa are to be thanked, not censured. But the canon of "silence equals death" applies here: We are ignoring a responsibility to defend the mass of innocent Western doctors against the belief that they are not treating disease, but intentionally spreading it. We should approach Africans' suspicions with respect, realizing that they are born of the acts of a few monsters and of the deadly constraints on medical care in difficult conditions. By continuing to dismiss their reasonable fears, we raise the risk of even more needless illness and death.

Harriet A. Washington is the author of "Medical Apartheid: The Dark History of Medical Experimentation on Black Americans From Colonial Times to the Present."

"Western medicine's two-faced history part of country's ARV tangle"

Date: 30 July 2007

Source: *Business Day (South Africa)*

Author(s): Jonny Steinberg

<http://allafrica.com/stories/200707300202.html>

On the first Sunday in February, City Press led its front page with dispiriting news about a clinical trial for a **microbicide**, an anti-HIV **vaginal gel**. The trial, which was being conducted in SA and other countries, was halted when it became clear that women using the product were contracting HIV at a faster rate than a control group using a placebo. Something had clearly gone awry.

When the story broke, I was in Lusikisiki in Eastern Cape spending time with the nurses and lay people who staff a phenomenally successful antiretroviral (ARV) treatment programme. In the days following the report, **microbicide** was the talk of every meeting I attended.

At a support group for people on ARVs, a Treatment Action Campaign (TAC) activist issued a warning about the gel. "It's on the shelf at the pharmacy opposite the Sasol garage," she said. "It says on the box that if you use this cream, you don't have to use condoms. That is a lie. There are people who want to kill us." "Is it also at Shoprite?" a woman asked. "Wherever you see this cream," the TAC activist replied, "don't buy it."

Later in the week I met the senior district official in charge of Aids treatment. A former nurse, she had been a primary health care manager for many years. "What have they done to these women?" she asked me. "They were told that if they used this gel they would not get HIV and now they are stuck with this terrible disease."

Wherever I went I was struck by the gulf between my understanding of what had happened and that of Lusikisiki's lay people and nurses. On the morning after the story broke, I listened on the radio to the head of the Medical Research Council explain that the women had been informed that the cream was in the trial stage, that they ought to keep using condoms, and, indeed, that they might be part of the placebo group and thus not be using a **microbicide** at all. To my mind, the ethics of the trial appeared to have been impeccable.

Among many of those I listened to in Lusikisiki, in contrast, it was instinctively understood that black women had been used and deceived, and that all black women were unsafe, even those who ventured innocently into the pharmacy on Lusikisiki's main road. Why is this story important? After years of bad faith, the government has finally put a serious Aids treatment plan on the table.

Correctly, it is envisaged that nurses and lay people are to play a frontline role in delivering treatment; the scale of the epidemic is so immense that if all treatment is doctor-led and hospital-based, most people in need of ARVs will die waiting for them. If nurses and lay people are to occupy the frontline, what sort of role will they play there?

Having spent 18 months speaking to people who staff a rural ARV programme at its grassroots, my sense is that their relation to medicine is extremely complicated. On one hand, most have either joined or been heavily influenced by SA's powerful treatment movement; they champion ARVs with a commitment that borders on the evangelical.

When a rumour erupts in an outlying village that this ARV deforms fetuses, or that one causes madness, lay people at the grassroots raise a powerful and articulate defence of Aids medicine. But another part of them, often cornered off and separate from their views on ARVs, carries an abiding suspicion of western medicine. It is a suspicion that resounds on every inch of the planet colonised by western imperial powers in the 19th century, from Eastern Cape to

Gujarat.

In Lusikisiki, for instance, it was widely rumoured during the first months of the town's ARV programme that the white doctor conducting HIV tests carried the virus in his needle. The rumour dissipated and the doctor was soon lauded, but the quick transition in his status from potential villain to hero has about it an aura of instability.

These inherited suspicions of the formerly colonised are grounded in generations of experience. The history of western medicine in Africa is an extremely ambiguous one. The idea that it is Janus-faced, that it can either heal or be used as a tool of callous experimentation, is deeply etched into African experience.

What I saw during that week in early February was a group of people who understood themselves to be both administrators of a lifesaving Aids medicine and potential victims of a racist and murderous Aids medicine. I do not think that ambiguity will ever be erased from the ranks of those who staff the frontline of this country's quest for Aids treatment; I imagine that stories like the one I heard in February are an indelible part of that quest.

Steinberg is a freelance journalist.

"Accessing NIH research"

Date: 27 July 2007

Source: *The Los Angeles Times*

Author(s): Editorial

<http://www.latimes.com/news/opinion/la-ed-nih27jul27,0,2419093.story?coll=la-opinion-leftrail>

Taxpayers pony up \$28 billion annually for the National Institutes of Health, the world's largest source of funding for medical research. The payoff, in addition to the occasional spectacular breakthrough, is more than 60,000 published studies each year. The first beneficiaries of that knowledge aren't doctors or patients. They are the publishers of the journals that review, print and sell the results to subscribers. Your tax dollars may have financed the clinical trial of a new treatment regime for the rare disease you've contracted, but you'll probably still have to pay to see the results.

Now, some lawmakers are trying to increase the public's access to this research. In a new funding bill for the NIH, the House of Representatives required that the results of the studies the government funds must be made freely available online within 12 months of their publication. The requirement builds on a 2-year-old NIH initiative to gather research in a free website called PubMed Central. That initiative was voluntary. But so few researchers complied -- less than 5% in the first year -- that proponents of "open access" to scientific research have lobbied to make it mandatory.

The main opposition has come from publishers, who argue that making research available free could ruin the smaller journals that serve some medical specialties. Libraries may stop subscribing to costly niche journals if they know the material will be available for free within a year. And if those journals die off, researchers will lose the valuable services they supply, such as rounding up experts to review studies before they're published.

While publishers have an important role to play, particularly in judging a study's credibility, that doesn't mean they're entitled to squeeze cash from that study in perpetuity. An open access requirement could force changes in some journals' business models, but a growing number have found ways to succeed while making research available for

free -- for example, by charging researchers fees for publication. And the 12-month period of exclusivity enables publishers to continue selling journals to those with the most immediate need to see them.

At the same time, opening up access to NIH-funded studies will increase their impact on researchers around the world. That's very much in the public interest. The more information that's available, the more chance someone will leverage it into another medical breakthrough.

"Hotels told to provide condoms"

Date: 27 July 2007

Source: *Reuters*

<http://www.reuters.com/article/lifestyleMolt/idUSPEK27213320070727>

China has ordered all hotels, holiday resorts and public showers to provide condoms, part of nationwide efforts to fight the spread of AIDS, a newspaper said on Friday. The regulation, issued by the commerce and health ministries, also required pamphlets about AIDS prevention to be displayed, the Beijing News said. The move follows an unusual step by the booming eastern province of Zhejiang in March to fine hotels and bars if they did not provide condoms.

China originally stigmatized AIDS as a disease of the decadent, capital West -- a problem of gays, sex workers and drug users. Traditionally, none of these officially existed in communist China. It has belatedly woken up to the problem and health experts have warned the virus is now moving into the general population. But a lack of sex education and unwillingness to talk about sex still hampers the fight, health experts say.

"China, India join WHO clinical trial registry system"

Date: 26 July 2007

Source: *Xinhua News Agency*

Author(s): Du Editor: Xiaodan

<http://www.cctv.com/english/20070726/108111.shtml>

China and India have joined the World Health Organization (WHO)'s clinical trial registry system in order to ensure the transparency and good quality of their research activities, the UN agency said on Wednesday. Both China and India have a rapidly expanding clinical trial research sector, WHO said in a statement. The inclusion of China and India in the WHO's online database for clinical trials is a major step for policymakers and scientists, who can now track local research activities, improve the quality of that research, and meet global standards for transparency, the statement said.

According to the statement, the Chinese Clinical Trial Register was established in 2005 and has now met the criteria to submit its trial registry data to WHO's web search portal. India's registry was created only recently and designed to ensure data meeting WHO reporting rules.

"The addition of these two clinical trial registers is a milestone in a growing international movement for more transparency and accountability in research involving people," said WHO's Director-General Dr Margaret Chan. "This development will contribute to improving the ethical conduct of, and public trust in clinical trials, which are vital for testing new life-saving treatments."

The WHO's online database on clinical trials was established in May to help doctors, patients, scientists and policy-makers track trials going on around the world. A number of countries, including the United States, Britain, Australia and New Zealand, have joined the registry system.

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8. ANNOUNCEMENTS

Deadline extended for lubricant survey

www.irmwg.org

The deadline for the International Rectal **Microbicide** Working Group's (IRMWG) Lubricant Survey has been extended to August 31! The survey's goal is to determine which products are most typically used for anal sex, and thus prioritize the next round of lubricants to be tested for anal safety. The results of this survey and subsequent testing will also give great insight into research currently being done on **microbicides** for rectal use. Links to the survey are in 6 languages and can be found on the IRMWG site at www.IRMWG.org. Congratulations to the International Rectal **Microbicides** Working Group (IRMWG) for their hard work and success on this survey!

From the desk of Dr. Elias Zerhouni

<http://www.nih.gov/about/director/newsletter/Summer2007.htm>

The Summer 2007 "From the Desk of Dr. Elias Zerhouni" Newsletter is a special issue on Peer Review. Please, take this opportunity to give NIH your thoughts at the link in the newsletter.

The Invisible Cure: Africa, the West, and the Fight Against AIDS

<http://www.nybooks.com/articles/20492?email>

The Invisible Cure: Africa, the West, and the Fight Against AIDS

by Helen Epstein

Farrar, Straus and Giroux, 326 pp., \$26.00

William Easterly, of the New York Review of Books, wrote a review of Epstein's new book, which can be accessed at the above website.

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