



ALLIANCE FOR MICROBICIDE DEVELOPMENT

18 July 2008, Volume 9, Number 28

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

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

Its purpose is to:

- Raise awareness around the broadest possible range of opinions and information about microbicides disseminated in scientific journals and the media; and
- Provide an objective basis for decision-making and evidence-informed advocacy.

Articles included in the Digest do not necessarily reflect the views of the Alliance. No press releases are included, however when information from a press release is picked up by the media, that coverage is included. To suggest material for inclusion, please contact digest@microbicide.org. The 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/cs/weekly_news_digest. 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. ALLIANCE UPDATES AND COMMUNITY NEWS

Applying social networking information technologies to the prevention of HIV infection

<http://www.amfar.org/cgi-bin/iowa/grants/rsrch/rfp.html?record=26>

amfAR, The Foundation for AIDS Research, is pleased to announce the availability of targeted support for social/behavioral research projects relevant to applying social networking information technologies to the prevention of HIV infection.

Funding will be available for:

Research Grants – \$100,000 direct costs plus up to 20% for indirect costs. The performance period for grants awarded under this RFP will be for one year starting January 1, 2009.

Fellowships – Each fellowship is funded at a total of up to \$125,000: A maximum of \$110,000 is allowed for personnel (salary and fringe benefits) and other research-related direct costs. It is expected that a fellow will devote the decided majority of his or her time to the approved fellowship project. Personnel costs supported by the fellowship must represent a minimum of 85% effort and be consistent with institution policy for other institution personnel of similar rank and title, regardless of source(s) of support.

An additional \$3,636 is provided to support attendance at amfAR-approved professional development activities, for a direct cost maximum of \$113,636. Institutional indirect costs may not exceed 10% of direct costs.

The period of performance for fellowships awarded under this RFP will be for two years starting January 1, 2009.

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EDITOR'S NOTE: *The full text of this RFP announcement is available at the above website.*

New Digest compilation and distribution method

www.microbicide.org

Beginning this week, the *Digest* will be generated and sent with a new tool through the Alliance's improved website. As we work through the kinks of this process, please let us know of any issues with the new *Digest* distribution.

2. MEDIA COVERAGE OF MICROBICIDES

"Pathologists believe they have pinpointed achilles heel of HIV"

Date: 16 July 2008

Source: *ScienceDaily*

Author(s): University of Texas Health Science Center at Houston

<http://www.sciencedaily.com/releases/2008/07/080715165520.htm>

Human Immunodeficiency Virus (HIV) researchers at The University of Texas Medical School at Houston believe they have uncovered the Achilles heel in the armor of the virus that continues to kill millions.

The weak spot is hidden in the HIV envelope protein gp120. This protein is essential for HIV attachment to host cells, which initiate infection and eventually lead to Acquired Immunodeficiency Syndrome or AIDS. Normally the body's immune defenses can ward off viruses by making proteins called antibodies that bind the virus. However, HIV is a constantly changing and mutating virus, and the antibodies produced after infection do not control disease progression to AIDS. For the same reason, no HIV preventative vaccine that stimulates production of protective antibodies is available.

The Achilles heel, a tiny stretch of amino acids numbered 421-433 on gp120, is now under study as a target for therapeutic intervention. Sudhir Paul, Ph.D., pathology professor in the UT Medical School, said, "Unlike the changeable regions of its envelope, HIV needs at least one region that must remain constant to attach to cells. If this region changes, HIV cannot infect cells. Equally important, HIV does not want this constant region to provoke the body's defense system. So, HIV uses the same constant cellular attachment site to silence B lymphocytes - the antibody producing cells. The result is that the body is fooled into making abundant antibodies to the changeable regions of HIV but not to its cellular attachment site. Immunologists call such regions superantigens. HIV's cleverness is unmatched. No other virus uses this trick to evade the body's defenses."

Paul is the senior author on a paper about this theory in a June issue of the journal *Autoimmunity Reviews*. Additional data supporting the theory are to be presented at the XVII International AIDS Conference Aug. 3-8 in Mexico City in two studies titled "Survivors of HIV infection produce potent, broadly neutralizing IgAs directed to the superantigenic region of the gp120 CD4 binding site" and "Prospective clinical utility and evolutionary implication of broadly neutralizing antibody fragments to HIV gp120 superantigenic epitope."

First reported in the early 1980s, HIV has spread across the world, particularly in developing countries. In 2007, 33 million people were living with AIDS, according to a report by the World Health Organization and the United Nations.

Paul's group has engineered antibodies with enzymatic activity, also known as abzymes, which can attack the Achilles heel of the virus in a precise way. "The abzymes recognize essentially all of the diverse HIV forms found across the world. This solves the problem of HIV changeability. The next step is to confirm our theory in human clinical trials," Paul said.

Unlike regular antibodies, abzymes degrade the virus permanently. A single abzyme molecule inactivates thousands of virus particles. Regular antibodies inactivate only one virus particle, and their anti-viral HIV effect is weaker.

"The work of Dr. Paul's group is highly innovative. They have identified antibodies that, instead of passively binding to the target molecule, are able to fragment it and destroy its function. Their recent work indicates that naturally

occurring catalytic antibodies, particularly those of the IgA subtype, may be useful in the treatment and prevention of HIV infection,” said Steven J. Norris, Ph.D., holder of the Robert Greer Professorship in the Biomedical Sciences and vice chair for research in the Department of Pathology and Laboratory Medicine at the UT Medical School at Houston.

The abzymes are derived from HIV negative people with the autoimmune disease lupus and a small number of HIV positive people who do not require treatment and do not get AIDS. Stephanie Planque, lead author and UT Medical School at Houston graduate student, said, “We discovered that disturbed immunological events in lupus patients can generate abzymes to the Achilles heel of HIV. The human genome has accumulated over millions of years of evolution a lot of viral fragments called endogenous retroviral sequences. These endogenous retroviral sequences are overproduced in people with lupus, and an immune response to such a sequence that resembles the Achilles heel can explain the production of abzymes in lupus. A small minority of HIV positive people also start producing the abzymes after decades of the infection. The immune system in some people can cope with HIV after all.”

Carl Hanson, Ph.D., who heads the Retrovirus Diagnostic Section of the Viral and Rickettsial Disease Laboratory of the California Department of Public Health, has shown that the abzymes neutralize infection of human blood cells by diverse strains of HIV from various parts of the world. Human blood cells are the only cells that HIV infects.

“This is an entirely new finding. It is a novel antibody that appears to be very effective in killing the HIV virus. The main question now is if this can be applied to developing vaccine and possibly used as a **microbicide** to prevent sexual transmission,” said David C. Montefiori, Ph.D., director of the Laboratory for AIDS Vaccine Research & Development at Duke University Medical Center. The abzymes are now under development for HIV immunotherapy by infusion into blood. They could also be used to guard against sexual HIV transmission as topical vaginal or rectal formulations.

“HIV is an international priority because we have no defense against it,” Paul said. “Left unchecked, it will likely evolve into even more virulent forms. We have learned a lot from this research about how to induce the production of the protective abzymes on demand. This is the Holy Grail of HIV research -- development of a preventative HIV vaccine.”

Major contributors to the research from the UT Medical School include Yasuhiro Nishiyama, Ph.D., and Hiroaki Taguchi, Ph.D., both with the Department of Pathology and Laboratory Medicine, and Miguel Escobar, M.D., of the Department of Pediatrics. Maria Salas and Hanson, both with the Viral and Rickettsial Disease Laboratory, contributed.

The research was funded by the National Institutes of Health and the Texas Higher Education Coordinating Board.

"Culture may impede microbicide uptake"

Date: 14 July 2008

Source: *Africa Renewal (United Nations)*

Author(s): Henry Neondo

http://africasciencenews.org/asns/index.php?option=com_content&task=view&id=551&Itemid=1

A recent study on **microbicides** among Ghanaian women reveal that while Ghanaian women would have a high level of interest in **microbicides**, with varying interest in formulas with different contraceptive and disease prevention properties, cultural factors however may impact on **microbicide** use.

These may often be related to gender and power issues.

According to the researchers, as **microbicides** are being developed, cultural issues and behavioral correlates will need to be assessed to help ensure acceptability and use.

In addition, they say gendered negotiation power and the implications of covert use need to be addressed in **microbicide** education and social marketing.

Vaginal **microbicides**, substances that may substantially decrease transmission of sexually transmitted infections (STI) including human immunodeficiency virus (HIV), are currently in clinical trials.

They are being presented as woman-initiated prevention methods that have the potential to be used without partners' knowledge.

However, it is recognised that covert use may be challenging, due to the accompanying increase in vaginal lubrication.

This study explored factors that may influence acceptability and utilisation of vaginal **microbicides** in Ghana, a sub-Saharan West African country with relatively low rates of HIV.

Qualitative research methods were employed in Accra, Ghana in 2005. Individual interviews were conducted with 10 staff working in reproductive health settings, and two focus groups were conducted with young women aged 24-28.

Three main topics emerged during the interviews and focus groups, including issues related to available contraceptive and prevention methods, perceptions of **microbicide** interest and acceptability, and cultural influences on **microbicide** acceptability and use.

Participants discussed issues associated with available contraceptive options that may influence **microbicide** uptake.

"Concept gels for biotech chief"

Date: 12 July 2008

Source: *The Age*

Author(s): Ari Sharp

<http://business.theage.com.au/concept-gels-for-biotech-chief-20080711-3dtm.html>

For new lovers, negotiating bedroom etiquette is tough at the best of times. What to do, what to wear, what to say, and, most importantly, how to keep safe. While health professionals have pushed for condoms to be a part of the sexual routine, in the throes of intimacy it can be a challenge for many women to get their partner to oblige.

Enter VivaGel, a product in development that promises to give women greater control over their sexual health. By applying the gel in the two hours before sex, women can protect themselves from genital herpes and HIV, as well as significantly reduce the chance of pregnancy.

While the lifestyle implications are significant in the developed world, it is in the developing world, particularly where HIV looms large, that the product could have a revolutionary impact.

The company behind the gel is Melbourne-based medical researcher Starpharma, led by its chief executive of two years, Jackie Fairley, a biotech veteran who includes stints at CSL and FH Faulding on her CV. (...)

EDITOR'S NOTE: *The full text of this article is available for public access at the above website.*

"Concept gels for biotech chief"

Date: 12 July 2008

Source: *The Age*

Author(s): Ari Sharp

Jackie Fairley was a vet but sawing and sewing were not for her, writes Ari Sharp.

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The company behind the gel is Melbourne-based medical researcher Starpharma, led by its chief executive of two years, Jackie Fairley, a biotech veteran who includes stints at CSL and FH Faulding on her CV.

The 45-year-old mother of two is one of a handful of women in senior positions in the industry. She brings to the role a brisk energy, takes a firm but polite approach and expects high standards of those around her.

"As the chief executive of a biotech company, in my view, you need to have a basic understanding of a whole lot of different disciplines," she says from her office at the Baker IDI research facility in Prahran. "Not necessarily to do the stuff yourself, but you have to be able to recognise bullshit when it's spun to you.

"You need to have an understanding of most of those issues because they're key drivers of success and if you don't have them adequately balanced, or if one of them doesn't stack up, then you can be seriously in trouble."

After studying science at the University of Melbourne, the high-achieving Fairley was given offers to study medicine and veterinary science at the university. She attributes her decision to study the care of animals rather than people on a rebellious streak, and said it shocked the dean of medicine, who could not recall anyone knocking back an offer to study at the prestigious medical school.

But her career as a vet lasted just a few years after the routine of surgery wore her down. "I'm not really that dexterous and I really didn't enjoy surgery a great deal. I wasn't particularly good at sewing and sawing."

The other thing that discouraged her was that the right thing to do and the cost-effective thing to do would often clash.

"You know that you could do A, B or C, and A would give you the best result. But no one would consider A because it was too expensive and B probably wouldn't be considered, so you were left with the third option, and I found that professionally frustrating."

The quandary that confronted the young vet two decades ago is similar to the one she will soon be grappling with in getting VivaGel to the mostly developing-world people who would benefit most from it.

The product is an antiviral gel that uses highly defined nanoparticles called dendrimers to zero in on a target.

Dendrimers - synthetic molecules, the surface of which can be covered with drug units - are Starpharma's speciality, and the relatively new science could be the next frontier not only in drug development, but in diagnostics and industrial technology.

But VivaGel is Starpharma's lead compound, and the company is going through clinical trials to test the gel's ability to prevent HIV, genital herpes and human papilloma virus. Just this week, the company said it was developing VivaGel as a treatment for bacterial vaginosis.

Just how it will fit into a couple's sexual routine is not completely certain. While the gel is an improvement on unprotected sex, it doesn't provide a shield against the full range of sexually transmitted diseases. It is also far from

foolproof as a contraceptive, offering about 80% certainty.

So, for now at least, it's likely most users would also want the assurance of their partner wearing a condom. For this reason, Starpharma has taken the step of partnering with SSL International, the makers of Durex condoms, to include the **microbicide** in one of its product lines.

As for the gel, Fairley cites market research showing that 30-40% of female US college students would buy a **microbicide**, such as VivaGel, and that jumps to 70% for one that also acts as a contraceptive. The strong response is a reflection of the growing spread of genital herpes, which affects 22% of sexually active adults in the US and is projected to rise to up to 50% by 2025.

Such is the expected surge in herpes in the US that the National Institutes of Health, the major government funder of health research, has contributed about \$US26 million (\$A27million) to Starpharma in an effort to turbocharge development of the product.

When Fairley joined Starpharma, VivaGel was already in development, but she says it was the promising nature of the technology, rather than just the potential to improve women's health, that attracted her.

"I think the product concept was an important factor in me joining the company, not because it was an empowering product or anything like that, but because it was a great product concept, and I think has enormous opportunity.

"And the fact that it addressed significant women's health issues is a bonus, I guess. But I guess the key driving factor was the strength I saw in the technology platform."

The biggest social impact of VivaGel is likely to be felt in places where the epidemic of HIV intersects with a cultural resistance to condoms. It's here that the discreet product (Fairley says partners often don't know it has been applied) can give women an effective way to protect themselves from disease.

"At the moment, there's really nothing. At the moment, for HIV, there are condoms, which are just not used in the developing world, even though they are given away for nothing. They're not used because of the mainly cultural barriers. There's abstinence, obviously, which George Bush is a proponent of, but it's not particularly effective.

Vaccines have not been effective for HIV, conventional wisdom is it will not be, and for herpes it's a similar story."

As is often the case, though, profits are hard to come by in medical products for the developing world. Poverty means users are unlikely to be able to pay for the product, so the need shifts to a third party to act as a buyer. The World Health Organisation and the Gates Foundation, the charitable fund started by Microsoft founder Bill Gates and his wife Melinda, come to mind, but the challenge will be persuading either to buy the gel with a commercially acceptable margin.

But if anyone can do it, it will be Fairley, whose tireless commitment to the company and its product has impressed many in the biotechnology industry. "She's somebody I think who's got a real sense of focus and discipline," says David Blake, editor of industry newsletter Bioshares. "She's got this kind of no-nonsense approach, which is attractive. She gets the job done."

"Researchers look at effectiveness of HIV prevention formats"

Date: 11 July 2008

Source: *Drug Delivery Insight*

Gilead Sciences is backing a major investigation that will compare the use of antiretroviral (ARV) tenofovir drugs for the treatment of HIV. The study will specifically look at the use of pill and **vaginal gel** formats and their effectiveness in preventing onset of the virus. For women, who make up nearly half of the 33 million people living with HIV/AIDS worldwide, the ARV tenofovir has shown particular promise because it can be formulated as either an oral tablet or a **vaginal gel** to be used daily. However, with ARV-based prevention approaches beset by a series of challenges, the

Microbicide Trials Network (MTN) aims to tackle the most pressing of these in the first clinical trial to directly compare the tablet and **vaginal gel** formulations of tenofovir.

The vagina is deemed an easy target for the virus because women are more than twice as likely as their male partners to acquire HIV through sexual intercourse. The clinical study, known as MTN-001, seeks to understand how each formulation of tenofovir works in the infection-prone cells, information that will help researchers determine the optimal doses needed to achieve drug concentrations most likely to prevent HIV in women. The study also looks to understand the factors that influence women's preferences for one daily approach over another, because not even the best approach will be effective if they are not used by women. Therefore, the Phase II study will evaluate women's adherence to and acceptance of three daily regimens of tenofovir - tenofovir gel, tenofovir disoproxil fumarate tablets and the two together - and the pharmacokinetics of each regimen. The study will enrol 144 sexually active HIV-negative women who will follow all three regimens, each for six weeks with one week between when no study product is used. A small number of participants from each site also will take part in in-depth interviews at the end of the 21-week study so researchers can collect more detailed information, including about women's adherence to and preferences between oral and vaginal formulations and between single and dual-use regimens. In the US, Case Western Reserve University in Cleveland and the University of Pittsburgh are now beginning to screen potential participants, which are expected to number 48 in total. Additional sites, including in South Africa and Uganda, will also be participating in the study, which is funded by the National Institute of Allergy and Infectious Diseases, a component of the US National Institutes of Health. Researchers expect to complete the study in 2009. In its tablet form, tenofovir disoproxil fumarate, known by the brand name Viread, is regarded as one of the most widely used regimens for treating HIV. The active ingredient in tenofovir belongs to a class of ARVs called nucleotide reverse transcriptase inhibitors (NRTIs), which act against HIV by targeting a key enzyme the virus needs to make a copy of its genetic material - an essential step for the virus to multiply and infect other cells. Tenofovir is being evaluated in clinical trials to determine if this first-line treatment can also prevent HIV when used every day by people who are HIV-negative, an approach known as pre-exposure prophylaxis (PrEP). As a **vaginal gel**, tenofovir is among a newer class of candidate **microbicides** with specific activity against HIV. MTN-001 is part of a portfolio of trials evaluating the oral and gel forms of tenofovir. Recently, MTN researchers launched the first trial in pregnant women, seeking to understand the extent that pregnancy affects how the body absorbs the active drug in the gel and whether the drug can be transferred to the fetus. The VOICE Study (Vaginal and Oral Interventions to Control the Epidemic), a trial involving 4,300 women that is expected to begin early 2009, will be the first effectiveness trial evaluating in the same study both a **microbicide** (tenofovir gel) and PrEP (oral tenofovir and oral Truvada, a combination of tenofovir disoproxil fumarate and another antiretroviral agent called emtricitabine). Both oral and **vaginal gel** formulations of tenofovir were developed by Gilead Sciences, which assigned a royalty-free licence for the topical gel to the International Partnership for **Microbicides** and Conrad in December 2006.

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3. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

"Using modeling to explore the degree to which a microbicide's sexually transmitted infection efficacy may contribute to the HIV effectiveness measured in Phase 3 microbicide trials"

Author(s): Vickerman P, Foss A, Watts C

Reference: J Acquir Immune Defic Syndr. 08 July 2008;Epub ahead of print.

<http://highwire.stanford.edu/cgi/medline/pmid;18614928>

Published Abstract: BACKGROUND:: Several **microbicide** candidates show activity against pathogens that cause sexually transmitted infections (STIs). This may increase a **microbicide**'s impact on HIV in phase 3 trials. Modeling is used to estimate the degree to which a **microbicide**'s STI efficacy contributes to the HIV effectiveness of a phase 3 **microbicide** trial. METHODS:: An expression is derived and coupled with an STI model to estimate how much a **microbicide**'s STI efficacy contributes to a trial's HIV effectiveness. The STI model estimates the decrease in STI prevalence that may occur in the trial's active gel arm for **microbicides** of different STI efficacy. Projections are produced for different STI cofactors and epidemiological settings. RESULTS:: The model projects that if a **microbicide** is active against curable STIs with a combined prevalence of $\geq 10\%$ among trial participants and the reduction in HIV incidence is $< 50\%$, then the STI activity could have substantially contributed to the trial's HIV effectiveness ($> 50\%$ in some cases) if the per exposure multiplicative STI cofactor is 2.5 or greater. However, if the STI prevalence is $< 10\%$ or the STI cofactor is < 2.5 or if the reduction in HIV incidence is $> 50\%$, then the trial's HIV effectiveness will be mainly due to its direct HIV efficacy. CONCLUSIONS:: In high STI settings, phase 3 trials documenting a moderate impact on HIV incidence may partially result from a gel's activity against curable STI. Care should be taken generalizing these trial results to other settings. This is less important for trials documenting large reductions in HIV incidence.

"Development and in vitro evaluation of chloroquine gels as microbicides against HIV-1 infection"

Author(s): Brouwers J, Vermeire K, Schols D, et al

Reference: Virology. 05 July 2008;Epub ahead of print.

<http://highwire.stanford.edu/cgi/medline/pmid;18606432>

Published Abstract: The potential success of a **microbicide** candidate in resource-poor countries will depend to a large extent on its availability and cost. Chloroquine is an inexpensive antimalarial drug that also exerts anti-HIV activity. The purpose of this study was to develop and characterize a vaginal formulation for chloroquine with preservation of its anti-HIV-1 activity. Gels containing the nonionic polymer hydroxyethyl cellulose were loaded with concentrations of the diphosphate salt of chloroquine (0.3-30 mg/g), that were 10(2)- to 10(4)-fold higher than typical in vitro anti-HIV-1 IC(50)-values of chloroquine (ca. 6 $\mu\text{g/ml}$). The gels were clear and homogeneous and displayed an osmolality of 300 mOsm/kg, a pH of 4.6 and a viscosity of 1.4 Pa s. Gel characteristics were preserved for at least 3 months at 40 degrees C and 75% relative humidity. Importantly, the chloroquine gels exerted a dose-dependent anti-HIV-1 activity in vitro (mean IC(50) from 23 to 0.4 mg gel/ml) and the intrinsic activity of chloroquine was not affected by formulation factors. The in vitro efficacy of the chloroquine gel formulations warrants further testing of this drug as an anti-HIV-1 **microbicide** candidate.

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http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6WXR-4SXS36M-1&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&

[_userid=10&md5=8ace3d0e61787223e52f57799d9976c7](#)

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"A summary of preclinical topical microbicide vaginal safety and chlamydial efficacy evaluations in a pigtailed macaque model"

Author(s): Patton D, Cosgrove Sweeney Y, Paul K

Reference: Sex Transm Dis. 02 July 2008;Epub ahead of print.

<http://highwire.stanford.edu/cgi/medline/pmid;18607310>

Published Abstract: BACKGROUND:: The development of topical **microbicides** represents a new and exciting field in the prevention of sexually transmitted diseases, and it is especially important that candidate products undergo rigorous preclinical safety and efficacy testing before advancing to clinical trials. METHODS:: We have developed a standardized protocol for preclinical vaginal safety and efficacy assessment of topical **microbicide** candidates in a

nonhuman primate model. Over 7 years of funding under an NIH contract, we evaluated a total of 28 test compounds for vaginal safety (via colposcopy, vaginal pH, and microflora) and 9 compounds for efficacy against cervical chlamydial infection. In this article, we describe our methods in detail and summarize our results, particularly noting the ability of our model to distinguish products with deleterious effects on the cervicovaginal environment. We also outline the specific criteria used to determine which products should move into efficacy trials and which should be recommended for reformulation to the manufacturer. **RESULTS::** Overall, we noted acceptable safety profiles for 24 of 28 candidate products. Common findings included a transient decrease in vaginal pH, petechiae, and mild erythema. Four products were associated with significant adverse colposcopic findings including blisters, epithelial abrasions, and friability; all 4 products were successfully reformulated and showed acceptable safety profiles at lower concentrations. No products showed complete protection against cervical chlamydial infection. **CONCLUSIONS::** The macaque preclinical safety and efficacy model is critical to maintaining the pace of topical **microbicide** development, which could ultimately offer a significant opportunity for intervention in the global HIV/AIDS epidemic.

"Perceptions of acceptability and utility of microbicides in Ghana, West Africa: A qualitative, exploratory study"

Author(s): Tanner EA

Reference: SAHARA J. 5(1):11-18.

<http://www.ajol.info/viewarticle.php?jid=197&id=40911>

Published Abstract:

Vaginal microbicides, substances that may substantially decrease transmission of sexually transmitted infections (STI) including human immunodeficiency virus (HIV), are currently in clinical trials. They are being presented as woman-initiated prevention methods that have the potential to be used without partners' knowledge. However, it is recognised that covert use may be challenging, due to the accompanying increase in vaginal lubrication. This study explored factors that may influence acceptability and utilisation of vaginal microbicides in Ghana, a sub-Saharan West African country with relatively low rates of HIV. Qualitative research methods were employed in Accra, Ghana in 2005. Individual interviews were conducted with 10 staff working in reproductive health settings, and two focus groups were conducted with young women aged 24-28. Three main topics emerged during the interviews and focus groups, including issues related to available contraceptive and prevention methods, perceptions of microbicide interest and acceptability, and cultural influences on microbicide acceptability and use. Participants discussed issues associated with available contraceptive options that may influence microbicide uptake. All respondents suggested that Ghanaian women would have a high level of interest in microbicides, with varying interest in formulas with different contraceptive and disease prevention properties. Cultural factors that may impact on microbicide use, often related to gender and power issues, were also discussed. Thus, as microbicides are being developed, cultural issues and behavioral correlates will need to be assessed to help ensure acceptability and use. In addition, gendered negotiation power and the implications of covert use need to be addressed in microbicide education and social marketing.

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4. PUBLISHED RESEARCH: RELEVANT BASIC AND TRANSLATIONAL SCIENCE

"Reduction in severity of a herpes simplex virus type 1 murine infection by treatment with a ribozyme targeting the UL20 gene RNA"

Author(s): Liu J, Lewin SA, Tuli SS, et al

Reference: Virology. 01 August 2008;82(15):7467-74.

<http://jvi.asm.org/cgi/content/abstract/82/15/7467?maxtoshow=&HITS=3&hits=3&RESULTFORMAT=&andorexactitle=&andorexacttitleabs=&andfulltext=microbicide%2C+microbicides&andorexactfulltext=or&searchid=1&usestrictdates=yes&resourcetype=HWCIT&ct>

Published Abstract:

Hammerhead ribozymes were designed to target mRNA of several essential herpes simplex virus type 1 (HSV-1) genes. A ribozyme specific for the late gene UL20 was packaged in an adenovirus vector (Ad-UL20 Rz) and evaluated for its capacity to inhibit the viral replication of several HSV-1 strains, including that of the wild-type HSV-1 (17syn+ and KOS) and several acycloguanosine-resistant strains (PAAr5, tkLTRZ1, and ACGr4) in tissue culture. The Ad-UL20 Rz was also tested for its ability to block an HSV-1 infection, using the mouse footpad model. Mouse footpads were treated with either the Ad-UL20 Rz or an adenoviral vector expressing green fluorescent protein (Ad-GFP) and then infected immediately thereafter with 10⁴ PFU of HSV-1 strain 17syn+. Ad-UL20 ribozyme treatment consistently led to a 90% rate of protection for mice from lethal HSV-1 infection, while the survival rate in the control groups was less than 45%. Consistent with this protective effect, treatment with the Ad-UL20 Rz reduced the viral DNA load in the feet, the dorsal root ganglia, and the spinal cord relative to that of the Ad-GFP-treated animals. This study suggests that ribozymes targeting essential genes of the late kinetic class may represent a new therapeutic strategy for inhibiting HSV infection.

"Duffy antigen receptor for chemokines mediates trans-infection of HIV-1 from red blood cells to target cells and affects HIV-AIDS susceptibility"

Author(s): He W, Neil S, Kulkarni H, et al

Reference: Cell Host and Microbe. 17 July 2008;4:52-62.

<http://www.cellhostandmicrobe.com/content/article/fulltext?uid=PIIS193131280800190X>

Published Abstract:

Duffy antigen receptor for chemokines (DARC) expressed on red blood cells (RBCs) influences plasma levels of HIV-1-suppressive and proinflammatory chemokines such as CCL5/RANTES. DARC is also the RBC receptor for *Plasmodium vivax*. Africans with *DARC 46C/C* genotype, which confers a DARC-negative phenotype, are resistant to *vivax* malaria. Here, we show that HIV-1 attaches to RBCs via DARC, effecting *trans*-infection of target cells. In African Americans, *DARC 46C/C* is associated with 40% increase in the odds of acquiring HIV-1. If extrapolated to Africans, 11% of the HIV-1 burden in Africa may be linked to this genotype. After infection occurs, however, DARC-negative RBC status is associated with slower disease progression. Furthermore, the disease-accelerating effect of a previously described *CCL5* polymorphism is evident only in DARC-expressing and not in DARC-negative HIV-1-infected individuals. Thus, DARC influences HIV/AIDS susceptibility by mediating *trans*-infection of HIV-1 and by affecting both chemokine-HIV interactions and chemokine-driven inflammation.

EDITOR'S NOTE: *The full text of this article is available for public access at the above website.*

"Imaging the biogenesis of individual HIV-1 virions in live cells"

Author(s): Jouvenet N, Bieniasz DP, Simon MS

Reference: Nature. 10 July 2008;454:236-240. doi:10.1038/nature06998

<http://www.nature.com/nature/journal/v454/n7201/abs/nature06998.html>

Published Abstract: Observations of individual virions in live cells have led to the characterization of their attachment, entry and intracellular transport¹. However, the assembly of individual virions has never been observed in real time. Insights into this process have come primarily from biochemical analyses of populations of virions or from microscopic studies of fixed infected cells. Thus, some assembly properties, such as kinetics and location, are either unknown or controversial^{2, 3, 4, 5}. Here we describe quantitatively the genesis of individual virions in real time, from initiation of assembly to budding and release. We studied fluorescently tagged derivatives of Gag, the major structural component of HIV-1—which is sufficient to drive the assembly of virus-like particles⁶—with the use of fluorescence resonance energy transfer, fluorescence recovery after photobleaching and total-internal-reflection fluorescent microscopy in living cells. Virions appeared individually at the plasma membrane, their assembly rate accelerated as Gag protein accumulated in cells, and typically 5–6 min was required to complete the assembly of a single virion. These approaches allow a previously unobserved view of the genesis of individual virions and the determination of parameters of viral assembly that are inaccessible with conventional techniques.

"The contents of the syringe"

Author(s): Salzberg S

Reference: Nature. 10 July 2008;454:160-161. doi:10.1038/454160a; Published online 9 July 2008

<http://www.nature.com/nature/journal/v454/n7201/full/454160a.html>

Published Abstract:

The influenza vaccine failed this winter. Steven Salzberg suggests that future success relies on sharing data more widely and making the virus strain selection process more transparent.

During the past 50 years, the scientific community has studied the influenza virus in great detail, and has developed an effective vaccine that is administered widely each year. The vaccine contains isolates from each of the three strains commonly circulating in humans: H3N2, H1N1 and influenza B. H3N2 has been the dominant strain of influenza A in most years, since it first emerged in 1968, and it is responsible for the most serious infections. The milder H1N1 has been co-circulating since it reappeared in Russia in 1977, and influenza B is milder yet. Because the virus mutates rapidly, the vaccine strains — especially H3N2 — need to be changed almost every year in order to remain effective. In some respects, the influenza-vaccine programme is a remarkable success: every year a new vaccine is developed and distributed, and most of the time it works.

This year, however, the vaccine was a failure: the strain of H3N2 that was used provided very little protection from infection. After a mild start dominated by H1N1 a new type of H3N2 emerged in mid-winter and quickly dominated, soaring to 71% of cases in the first 8 weeks of 2008 and overwhelming medical clinics in many places. A study in Wisconsin found the vaccine to be only 44% effective compared with the 70–90% effectiveness expected¹, and a Harris Poll of more than 2,500 people revealed that for the first time in at least four winters, people who were

vaccinated seemed no less likely to become infected². The harm was thus twofold; people fell ill and their trust in the vaccine system was undermined. This failure could have been predicted, if not prevented, through a more open system of vaccine design, a stronger culture of sharing in the influenza research community and a serious commitment to new technologies for production. The habits of the vaccine community must change for the sake of public health.

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EDITOR'S NOTE: *The full text of this article is available for public access at the above website.*

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5. PUBLISHED RESEARCH: RELEVANT BEHAVIORAL AND SOCIAL SCIENCE AND EPIDEMIOLOGY

"Alternatives to the randomized controlled trial"

Author(s): West S, Duan N, Pequegnat W, et al

Reference: Am J Public Health. 01 August 2008;98(8):1359-1366.

<http://www.ajph.org/cgi/content/abstract/AJPH.2007.124446v1>

Published Abstract:

Public health researchers are addressing new research questions (e.g., effects of environmental tobacco smoke, Hurricane Katrina) for which the randomized controlled trial (RCT) may not be a feasible option. Drawing on the potential outcomes framework (Rubin Causal Model) and Campbellian perspectives, we consider alternative research designs that permit relatively strong causal inferences. In randomized encouragement designs, participants are randomly invited to participate in one of the treatment conditions, but are allowed to decide whether to receive treatment. In quantitative assignment designs, treatment is assigned on the basis of a quantitative measure (e.g., need, merit, risk). In observational studies, treatment assignment is unknown and presumed to be nonrandom. Major threats to the validity of each design and statistical strategies for mitigating those threats are presented.

"Next stop, don't block the doors: opening up access to clinical trials results"

Author(s):

Reference: PLoS Med. 15 July 2008;5(7):e160. Editorial

<http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0050160>

Published Abstract:

2008 has been a good year for access to research. Effective New Year's Day, both the Canadian Institutes of Health Research [1] and the Howard Hughes Medical Institute [2] require publicly accessible archiving of papers published by their grantees. Also in January, the European Research Council announced its European Union-wide open-access mandate [3]. In February, the Harvard Faculty of Arts and Sciences voted to give the University a worldwide license to exercise copyright in each faculty member's scholarly articles for the purpose of making these articles freely available [4]; Harvard Law School committed to mandatory free access in May [5]. In March, the European University Association endorsed open-access repositories [6], and in April the United States National Institutes of Health Public Access Policy [7] took effect, bringing America's leading sponsor of biomedical research into the

impressive circle of agencies that require archiving of papers resulting from the research they fund. Judging by the ever-increasing number of submissions to PLoS journals, authors appear to be voting with their manuscripts for open access to research.

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EDITOR'S NOTE: The full text of this article including references is available for public access at the above website.

"The role of men in women's acceptance of an intravaginal gel in a randomized clinical trial in Blantyre, Malawi: a qualitative and quantitative analysis"

Author(s): Salter M, Go V, Celentano D, et al

Reference: AIDS Care. 05 June 2008;;1-10. Epub ahead of print.

<http://highwire.stanford.edu/cgi/medline/pmid;18608053>

Published Abstract: Survey questionnaires and focus group discussions were used to investigate the association between a female participant's acceptance and her perception of her male partner's acceptance of an intravaginal gel as a prototype **microbicide**. Women who perceived their male partners would accept using the gel were more likely to highly accept the gel as compared to women who perceived their male partners would not accept using the gel (OR =24.57; 95%CI: 16.49-36.61). Qualitative analysis supported a positive association between female acceptability and perceived male partner acceptability. Qualitative research reiterated this finding and also found that men and women had different approaches to assess gel acceptability. Women integrated perceptions of their partner's acceptance into their own acceptability and reported their partners had positive experiences. In contrast, men reported a more neutral experience with the gel and assessed the gel without overt consideration of their partner's experiences. These results indicate that female perceptions of male partner acceptability and actual male partner acceptability need to be considered when addressing female-controlled product acceptability and use.

"Costing adult male circumcision in high HIV prevalence, low circumcision rate countries"

Author(s): Fieno J

Reference: AIDS Care. 01 May 2008;20(5):515-520.

<http://www.informaworld.com/smpp/content~content=a793185562~db=all~jumptype=rss>

Published Abstract:

The dramatic evidence that male circumcision has a substantial effect in preventing HIV infection might be the most important medical finding in the course of the AIDS epidemic since the introduction of highly active antiretroviral therapy (HAART). The transition from clinical trials to implementation of a general adult male circumcision (AMC) program is beginning, and this paper uses an AMC cost model (in Microsoft Excel) to estimate the cost of a rapid scale-up of an AMC program in Mozambique, a country with a generalized epidemic and low rate of male circumcision. There are three major findings: (1) Even the most modest of AMC programs would place great stress on human resources, and task-shifting might lead to more accidents or adverse events that would increase the cost per AMC. (2) The fiscal burden of AMC is surprisingly low, but a rapid scale-up of AMC poses additional fiscal stress for Mozambique's already under-funded public health system. (3) AMC as an HIV prevention tool is very robust in terms of its cost-effectiveness in Mozambique, even at a high AMC accident or complication rate. Any AMC roll-out in Mozambique would face severe constraints in the health system (namely human resources) that would likely limit the

scale of an AMC program and perhaps its effectiveness against its generalized epidemic.

"Male circumcision is not the HIV 'vaccine' we have been waiting for!"

Author(s): Green L, McAllister R, Peterson K, et al

Reference: Future HIV Therapy. 01 May 2008;2(3):193-199.

<http://www.futuremedicine.com/doi/full/10.2217/17469600.2.3.193?prevSearch=allfield%3A%28male+circumcision%29>

Published Abstract:

Over the past several months, some researchers and health organizations [101] have proclaimed circumcision to be a compelling and important new HIV tool. A recent commentary claims that circumcision is “at least as good as the HIV vaccine we have been waiting for, praying for and hoping to see in our lifetimes” [1]. Thousands of African men now line up to get circumcised in the mistaken belief that it will save them from HIV, as some developing nations – lacking even rudimentary medical care and clean drinking water – rush to implement mass circumcision programs with encouragement and millions of pledged dollars from the US government [2,102,103]. In addition, there are calls for implementing mass neonatal circumcision [104].

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EDITOR'S NOTE: The full text of this article including references is available for public access at the above website.

"Assessing microbicide acceptability: a comprehensive and integrated approach"

Author(s): Morrow K, Ruiz M

Reference: AIDS Behav. 01 March 2008;12(2):1090-7165.

<http://www.springerlink.com/content/30u617k8j2203703/>

Published Abstract: A safe, effective, and acceptable **microbicide** is needed in order to decisively impact the global AIDS pandemic. As such, **microbicide** acceptability research is of paramount importance. In order to best utilize limited financial resources and save precious development time, acceptability studies should be fully integrated into preclinical and clinical trial contexts where candidate products are being developed and tested. An integrated approach for examining theoretically valid and relevant variables is needed so that data across studies and products can more effectively advance the field. We propose an approach for measuring factors related to **microbicide** acceptability in each phase of product development, and dependent on what product-specific knowledge is already established in the field. We discuss the roles that behavioral and social science methodologies should play in all phases of **microbicide** development, as well as the challenges faced when conducting acceptability research in the context of preclinical and clinical trial settings.

"Is male circumcision as good as the HIV vaccine we've been waiting for?"

Author(s): Klausner J, Wamai R, Bowa K, et al

Reference: Future HIV Therapy. 01 January 2008;2(1):1-7.

<http://www.futuremedicine.com/doi/full/10.2217/17469600.2.1.1?prevSearch=allfield%3A%28male+circumcision%29>

Published Abstract:

What would the reaction of the international public health community have been if a year ago scientists had announced the discovery of a vaccine or chemical gel that, in three separate clinical trials, had reduced the risk of heterosexual HIV infection in men by at least 60%? Considering that even with increasing access to antiretroviral therapy AIDS continues to be a huge killer - ever day over 2000 men become infected with HIV in sub-Saharan Africa alone, which eventually also results in millions of new cases in their partners and children - would not such an announcement have surely sparked a massive surge of excitement and renewed investment in HIV prevention? In fact, in December 2006 officials from the US NIH did announce the discovery of an intervention at least as effective, for heterosexual transmission, as the long hoped for AIDS vaccine. However, unlike many previous breakthroughs in medicine, this time the intervention was not discovered by a team of scientists toiling in academic or government laboratories. Rather, some two decades ago anthropologists, demographers and epidemiologists initially noticed, and then eventually proved beyond a reasonable doubt, that male circumcision (MC) very significantly reduces the risk of heterosexual HIV infection in men.

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EDITOR'S NOTE: The full text of this article is available for public access at the above website.

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6. EPIDEMIOLOGY

"Gene variant common in Africa ups HIV risk: study"

Date: 16 July 2008

Source: *Reuters*

Author(s): Will Dunham

<http://www.reuters.com/article/healthNews/idUSN1638188120080716?feedType=RSS&feedName=healthNews>

A gene variant that emerged thousands of years ago to protect Africans from malaria may raise their vulnerability to HIV infection but help them live longer once infected, researchers said on Wednesday.

The findings could help explain why AIDS has hit Africa harder than all other parts of the world.

People with the version of the gene have a 40 percent higher risk of becoming infected with the human immunodeficiency virus, or HIV, researchers in the United States and Britain wrote in the journal *Cell Host & Microbe*.

In Africa, the gene variant may account for 11 percent of HIV infections, the researchers said.

Sexual behavior and other social factors cannot completely explain why more than two-thirds of the world's 33 million people infected with HIV live in sub-Saharan Africa, the researchers said. So genes may be playing a pivotal role.

The gene in question controls a protein on the surface of red blood cells.

But even as it elevates a person's susceptibility to HIV infection, having this version of the gene seems to slow the progression of AIDS. Those with the variant who have been infected with HIV live roughly two years longer than people who do not have it, the researchers said.

"Nelson Sewankambo: building HIV/AIDS research in Uganda"

Author(s): Kapp C

Reference: Lancet. 05 July 2008;372(9632):21. Profile.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673608609770/fulltext>

Published Abstract:

In the early 1980s, two young Ugandan doctors decided to investigate the increasing phenomenon of diarrhoea and wasting, or so-called slim disease. It turned out to be the same disease that was spreading among homosexual men in the USA, and marked the start of Nelson Sewankambo's long battle against HIV/AIDS in Africa.

Sewankambo, Dean of Medicine at Makerere University, Uganda, was a founding investigator on the Rakai Project, one of the world's best established HIV/AIDS epidemiological studies. He was also co-founder of the Academic Alliance for AIDS Care and Prevention in Africa, linking Canadian, European, and Ugandan academics, and its pioneering Infectious Diseases Institute. "He's one of the real heroes of the African AIDS response", says Warner C Greene, Director of the Gladstone Institute of Virology and Immunology and Professor of Medicine, Microbiology and Immunology at the University of California, San Francisco. "He's a remarkable man. Very understated, very humble but razor sharp and incredibly effective", said Greene, who is also President of the Accordia Global Health Foundation, which evolved from the Academic Alliance and aims to boost health-care capacity and strengthen academic medical centres in Africa.

Sewankambo and his colleague David Serwadda attracted international scientific attention when they published a 1985 study in this journal about slim disease, focusing on the startlingly high rates of infection among sexually active adults in Rakai, a rural district near the Tanzanian border. The findings were initially greeted with scepticism, but Sewankambo and Serwadda persevered in trying to acquire funding for a community-based study.

In 1987, Columbia University summoned researcher Maria Wawer from vacation in Italy to go to Uganda and "talk to these guys". It was just 1 year after the end of internal strife and Entebbe airport still bore the scars of war. Patients at the main hospital in Kampala were lying on the floor and medicines were very scarce. "All this time, I'm thinking, 'I am out of here'", recalled Wawer, professor at the Johns Hopkins Bloomberg School of Public Health and the Columbia University Mailman School of Public Health. But she changed her mind after meeting Sewankambo and Serwadda and returned to the USA determined to collaborate with them to secure the necessary finance. "There was no beating about the bush and it was like a breath of fresh air. They said 'there is a job that needs to be done and we can work on it together'."

The Rakai Project became the Rakai Health Sciences Program and ballooned from a small community-based study to an international epidemiological treasure trove. The programme is now a collaboration of the Ministry of Health's Uganda Virus Research Institute, Makerere University, Johns Hopkins Bloomberg School of Public Health, and Columbia University, with 400 Ugandan staff and a regular cohort of 12

000 people. Last year startling results of trials in Rakai, South Africa, and Kenya convinced WHO and UNAIDS to recommend that governments embrace male circumcision as part of national HIV/AIDS prevention policy. Ronald Gray, professor at Johns Hopkins University's Department of Population and Family Health Sciences, said the Rakai team was "absolutely bowled over" by the results. Many other projects are currently on the go, ranging from basic

laboratory science all the way to research to enable the scale-up of circumcision, which remains complex and costly for most African countries. "It's been a phenomenal collaboration in terms of science, collegiality, and friendship", comments Gray, who jokingly rues that he helped refine Sewankambo's tastes from Ugandan beer and mixed blend whisky to single malts, making the cost of celebrating their successes ever more expensive. These international collaborations also mean that Sewankambo spends one quarter of his time travelling abroad, collaborating with an impressive list of US and European academic institutions. Sewankambo's two children are also abroad, studying in the USA and Canada, but "will have nothing to do with medicine", he says.

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EDITOR'S NOTE: *The full text of this article is available with a free subscription at the above website.*

"Trends in HIV incidence in homosexual men in developed countries"

Author(s): Grulich A, Kaldor J

Reference: Sex Health. 02 June 2008;5(2):113-118.

<http://www.publish.csiro.au/paper/SH07075.htm>

Published Abstract:

Objectives: To describe trends in HIV notifications and in other measures of HIV incidence in homosexual men in developed countries. **Methods:** A literature search was conducted using PubMed. In addition to the peer-reviewed literature, data on HIV surveillance trends were sought by searching websites of surveillance authorities in developed countries. **Results:** The availability of long-term HIV surveillance data varied considerably. However, in almost all jurisdictions in which such data were available, notifications of new HIV diagnoses among homosexual men have increased, mostly since the late 1990s. The magnitude of this increase varied, but was more than 50% in many countries. There were much fewer data available on trends in direct measures of HIV incidence in homosexual men, and increases in HIV testing rates may have contributed to the increases in HIV diagnoses in many countries. However, since the late 1990s, several clinic- and community-based cohort studies in Europe and North America reported increasing incidence. **Conclusion:** There were increases in HIV notifications in homosexual men in almost all developed countries, starting in the late 1990s and continuing to 2006. Although increases in HIV testing probably contributed to the increases in some settings, limited cohort data do support the existence of a true increase in HIV incidence in European and North American countries. Improved monitoring of HIV incidence in homosexual men at the population level is required to allow more timely assessment of the drivers underlying such trends.

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7. HIV/AIDS VACCINES

"Russia could develop HIV/AIDS vaccine within 10 to 15 years, health ministry official says"

Date: 14 July 2008

Source: *Kaiser Daily HIV/AIDS Report*

http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=53261

Russia could develop an HIV/AIDS vaccine within the next 10 to 15 years, Alexander Goliusov, HIV/AIDS controller for the country's consumer rights regulator, said Thursday during a video teleconference between Moscow and New Delhi, RIA Novosti reports. In addition, B.S. Banerji of the HIV/AIDS department at India's Ministry of Health and Family Welfare said that Indian scientists could develop a vaccine within a similar timeframe.

According to Goliusov, the Russian government has allocated more than one billion Russian rubles, or about \$42.7 million, for HIV/AIDS vaccine development. In addition, three research centers in St. Petersburg, Moscow and Novosibirsk have been incorporated into a vaccine development team, and study participants in St. Petersburg have been selected, Goliusov said. He added that the country has vaccine candidates "but there is still a lot of work to do."

Marina Shevyreva -- deputy head of human well-being, science and research at Russia's Ministry of Health and Social Development -- said the timeframes provided by the consumer rights regulator to develop a vaccine coincide with the health ministry's estimates (RIA Novosti, 7/10).

""Therapeutic' HIV vaccine leads to higher viral load, less time off treatment"

Date: 10 July 2008

Source: *AIDSmap.com News*

Author(s): Gus Cairns

<http://aidsmap.com/en/news/145514C7-B760-4902-8C36-F67F37BADC0B.asp>

In another blow to HIV vaccine development, a study published in the journal AIDS reports that a therapeutic vaccine given to people already living with HIV actually increased viral loads and reduced time off treatment - the opposite of what had been hoped. Higher doses of the vaccine - ALVAC 1452 - produced worse effects.

These results are especially puzzling and disappointing as studies with a similar therapeutic vaccine, sometimes combined with the immune booster interleukin-2, have had the opposite effect. In a study by the French vaccine pioneer Yves Levy, for instance, the viral load in subjects given the similar ALVAC 1433 vaccine ended up ten times lower than in subjects given placebo, and subsequent time off antiretroviral therapy (ART) was increased by 40% - see this report.

The authors of the current study say their results may be down to bad luck; a post-hoc analysis, for instance, found a higher proportion of "slow progressors" in the placebo group and of "fast progressors" in the vaccine group. But other initial analyses suggest that instead of stimulating lots of anti-HIV CD8 cells, which would kill HIV-infected cells, the vaccine mainly stimulated the formation of HIV-specific CD4 cells – which would only serve as targets for more HIV replication.

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EDITOR'S NOTE: *The full text of this article is available for public access at that above website.*

""Catalytic antibodies to HIV: Physiological role and potential clinical utility"

Author(s): Planquea S, Nishiyama Y, Taguchi H, et al

Reference: Autoimmunity Reviews. 01 June 2008;7(6):473-479.

http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6W8V-4SD1B9V-1&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=0b6b6e3f05385a42956026f4a48c5f77

Published Abstract:

Immunoglobulins (Igs) in uninfected humans recognize residues 421–433 located in the B cell superantigenic site (SAg) of the HIV envelope protein gp120 and catalyze its hydrolysis by a serine protease-like mechanism. The catalytic activity is encoded by germline Ig variable (V) region genes, and is expressed at robust levels by IgMs and IgAs but poorly by IgGs. Mucosal IgAs are highly catalytic and neutralize HIV, suggesting that they constitute a first line of defense against HIV. Lupus patients produce the Igs at enhanced levels. Homology of the 421–433 region with an endogenous retroviral sequence and a bacterial protein may provide clues about the antigen driving anti-SAg synthesis in lupus patients and uninfected subjects. The potency and breadth of HIV neutralization revives hopes of clinical application of catalytic anti-421–433 Igs as immunotherapeutic and topical **microbicide** reagents. Adaptive improvement of anti-SAg catalytic Igs in HIV infected subjects is not customary. Further study of the properties of the naturally occurring anti-SAg catalytic Igs should provide valuable guidance in designing a prophylactic vaccine that amplifies protective catalytic immunity to HIV.

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8. OTHER PREVENTION APPROACHES

"Ready for avian flu?"

Author(s): Yamada T, Dautry A, Walport M

Reference: Nature. 10 July 2008;454:162. doi:10.1038/454162a; Published online 9 July 2008

<http://www.nature.com/nature/journal/v454/n7201/full/454162a.html>

Published Abstract:

Committing to a vaccine stockpile is just the beginning. Tadataka Yamada, Alice Dautry and Mark Walport offer a roadmap for heading off a global avian influenza catastrophe.

Several chilling considerations highlight the seriousness of an impending pandemic of the H5N1 'avian' influenza virus. The highly contagious nature of influenza, the limited ability to restrict its transmission and the efficiency of modern international transport all conspire to reduce the time from the first infection to a potential global crisis. Recent models built on data from the 1918 flu pandemic predict that 50 million–80 million people could die¹. Perhaps not surprisingly, 95% of these deaths are likely to occur in the developing world, where higher population density, poor health status and limited access to public-health interventions prevail. Prevention through vaccination would be optimal, but vaccines against a pandemic strain might take six months to manufacture and deliver, even in developed countries. Moreover, total global capacity for flu vaccine manufacture in the first 12 months is estimated at only 500 million doses, and no global financing-vehicle exists.

There is some good news. The World Health Organization (WHO) has announced plans to stockpile H5 influenza vaccine and several manufacturers have already offered to contribute. Other manufacturers are supportive but await details before committing. Efforts have been initiated by the WHO to create a policy framework for vaccine allocation

and recommendations for its use. An ethics framework, and financing, regulatory and distribution systems will also have to be developed with member states.

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EDITOR'S NOTE: *The full text of this article is available for public access at the above website.*

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9. POLITICS AND POLICY

"G8 meeting disappoints on global health"

Author(s): McCurry J

Reference: Lancet. 19 July 2008;372(9634):191-194.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673608610545/fulltext>

Published Abstract:

Despite the confirmation of financial commitments for infectious diseases and health systems at the G8 meeting in Japan last week, campaigners were left cold by the lack of fresh pledges on other key issues, such as maternal and child health and water and sanitation. Justin McCurry reports.

A combination of mild optimism and dismay greeted the pledges on health and African development made at last week's G8 meeting in Japan. The mixed response came in the context of mounting concern that the world's wealthiest countries are renegeing on commitments made towards meeting the health-related Millennium Development Goals (MDGs) agreed by the group in Gleneagles, Scotland, 3 years ago.

In this year's communiqué, after 3 days of talks in Lake Toya, Toyako, the G8 leaders from Canada, France, Germany, Italy, Japan, Russia, the UK, and the USA recommitted themselves to doubling overseas aid to US\$50 billion by 2010, half of which will go to Africa.

Fears that the G8 would fail to set a deadline for increasing health spending by at least \$60 billion—agreed last year in Heilingendamm, Germany—proved unfounded after the leaders signed up to a 5-year programme to tackle infectious diseases and improve health systems in developing countries.

In their communiqué, the G8 leaders said they were “determined to honor in full their specific commitments to fight infectious diseases, namely malaria, tuberculosis, polio and working [sic] towards the goal of universal access to HIV/AIDS prevention, treatment and care by 2010”—a reaffirmation welcomed by WHO. (...)

"Senate agrees to \$50 billion AIDS plan"

Date: 17 July 2008

Source: *The Washington Post*

Author(s): Paul Kane

<http://www.washingtonpost.com/wp-dyn/content/article/2008/07/16/AR2008071602571.html>

The Senate approved legislation yesterday that would triple funding to fight AIDS and other diseases around the globe, rejecting efforts to pare down the bill's \$50 billion price tag.

On an 80 to 16 vote, the Senate dramatically increased the U.S. contribution to a global fund to combat AIDS, tuberculosis and malaria. President Bush, who requested \$30 billion over the next five years, has agreed to the larger amount for a program he started in 2003.

"We've made tremendous strides, but our work is not nearly finished. Two million people died last year of HIV-AIDS. Over two and a half million people died of malaria and TB," said Senate Foreign Relations Committee Chairman Joseph R. Biden Jr. (D-Del.). He praised Bush's "bold" support for AIDS funding, launched in the 2003 State of the Union address, calling it his greatest achievement as president.

Once a politically contentious issue, fighting AIDS has become popular at both ends of the ideological spectrum. During the debate, Sen. John F. Kerry (Mass.), the 2004 Democratic presidential nominee, praised former senator Jesse Helms (R-N.C.), a conservative icon who died July 4, for his decision in 2000 to support global AIDS funding.

Some Senate conservatives were divided over supporting the costly program, though they acknowledged its success.

"This is by far the only true foreign policy program that's working. The dollars are actually making a difference," said Sen. Tom Coburn (R-Okla.), a staunch opponent of most government spending.

"HIV is a death sentence, no question about it. If you go untreated, you're going to die," Coburn added.

According to the Office of the U.S. Global AIDS Coordinator, the money has provided services in poor nations that have prevented 194,000 HIV infections among infants.

But Sen. John Cornyn (R-Tex.) said the funding should have been reduced to \$35 billion over five years. He noted that the initial program cost \$15 billion.

"There should be a limit," Cornyn said. "It's one thing to say you'll support it at \$15 billion; it's another thing to say you'll support it at \$35 billion. To me, it's entirely another thing to support it at \$50 billion."

Cornyn was one of 16 Republicans to oppose the bill. Amendments to reduce its cost were rejected by large bipartisan majorities.

The program originally focused on 15 poor nations, but the legislation would expand it to help provide prevention and treatment services in more than 100 countries.

The House has passed its own version of the bill, but Biden said there are only minor differences between the two and

predicted a final version would soon be crafted and sent to the president for his signature.

One key difference in the bills is a House provision that would allow funding for family planning programs in poor nations.

"Senate passes bill to boost global AIDS funds"

Date: 16 July 2008

Source: *Reuters*

Author(s): Richard Cowan

<http://africa.reuters.com/wire/news/usnN16328689.html>

The Senate, fending off opposition from some conservative Republicans, voted on Wednesday to spend \$48 billion to fight AIDS worldwide over the next five years.

By a vote of 80-16, the Senate passed the legislation and ended weeks of delays orchestrated by some Republicans who thought the measure spent too much and objected to other provisions.

"In 2003, President Bush and this Congress launched the largest public health program in the history of the world," said Senate Foreign Relations Committee Chairman Joseph Biden, a Delaware Democrat, who pushed the legislation. "It is saving lives, millions of them."

The House of Representatives passed its version of the bill on April 2. The House and Senate will have to work out their differences to craft a final version.

"With passage of today's bill we are one step closer to ensuring that this excellent program continues to help those in need. I encourage the full Congress to move quickly to send me final legislation that I can sign," President George W. Bush said in a statement.

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EDITOR'S NOTE: *The full text of this article is available for public access at the above website.*

"160 groups lobby for lifting of US entry ban against foreigners with HIV"

Date: 14 July 2008

Source: *AAAS Policy Alert*

Author(s): Joe DeCapua

<http://www.voanews.com/english/Africa/2008-07-14-voa21.cfm>

About 160 organizations have joined forces to call for the lifting of a travel ban on HIV positive people, who want to come to the United States. The organizations want the US Senate to lift the ban as part of legislation to re-authorize PEPFAR, the Presidents Emergency Plan for AIDS Relief.

Mitchell Warren is head of the AIDS Vaccine Advocacy Coalition, one of the groups lobbying the senate. From New York, he spoke to VOA English to Africa Service reporter Joe De Capua about why the travel ban should be lifted.

"It's important for at least two reasons. One, it's just the wrong policy. There's no scientific evidence or good rationale to continue this ban. It was established back in 1987. There are only 12 countries left that still have this kind of travel ban. It includes Iraq, Saudi Arabia, South Korea, Sudan. And this is not a policy that works. And the second reason...is it is actually setting us back in terms of leadership in the fight against AIDS. When we think about the

number of researchers, of community advocates in other countries, who are HIV positive, who cannot come to this country, generally for their own work, it's absurd. And for over a decade now, we've not had international AIDS conferences taking place in the United States because of a decision made early on that no country that has a policy like this should be the host of one of the international conferences," he says.

Many HIV positive activists, including Africans, have expressed anger over the travel ban, saying they want to attend scientific meetings and other gatherings on HIV/AIDS in the United States.

Warren says, "With the advent of the PEPFAR program...the US government is showing great leadership when it comes to prevention and treatment. Certainly, the enormous amount of resource put to research from the United States government, NIH (National Institutes of Health) and other mechanisms, this country is a leader in the fight against AIDS. And to not allow our partners from all over the world, who happen to be HIV positive, to be able to engage with their peers and counterparts in this country really does set the process back. Sets the fight against AIDS back. And really detracts from what should be much more comprehensive leadership from the US government."

The US House of representatives has passed the PEPFAR reauthorization act. However, it's stalled in the senate, in part, because of the provision lifting the travel ban.

"HIV remains the only disease in the Immigration and Nationality Act that makes it inadmissible for entry in the United States. It's the only medical condition included," he says.

The legislation would give authority back to the Department of Health and Human Services, allowing it to decide on a case-by-case basis who with HIV can enter the country.

"Senate set to debate global AIDS relief"

Date: 14 July 2008

Source: *The Washington Times*

Author(s): Sean Lengell

Senators on Monday will take up a \$50 billion package to fight AIDS globally, despite some Republican concerns the bill could divert money to unrelated programs.

The upper chamber on Friday voted 65-3 to proceed to a final vote to fund the President's Emergency Plan for AIDS Relief (PEPFAR) for another five years. President Bush started the program in 2003 to combat HIV/AIDS, malaria and tuberculosis in Africa and other afflicted parts of the world.

The House overwhelmingly passed a similar bill in early April, but resistance from a handful of conservative Republican senators had kept it off the Senate floor until now. The current act expires at the end of September. A main sticking point is a current program mandate that requires 55 percent of the money go to treatment programs. Writers of the new bill dropped the provision, arguing that health care workers on the ground - not Washington politicians - can better determine what programs are most effective.

But Sen. Tom Coburn, Oklahoma Republican and a longtime supporter of PEPFAR, has spearheaded an effort to get the requirement restored, saying the mandate is necessary to prevent money from getting diverted into unrelated development and poverty-relief programs.

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EDITOR'S NOTE: *The full text of this article is available for public access at the above website.*

"Global health and the G8-is power just too sweet to share?"

Author(s): MacDonald R, Horton R

Reference: Lancet. 12 July 2008;372(9633):99-100.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673608610041/fulltext>

Published Abstract:

On July 8, at the Hokkaido Toyako Summit in Japan, G8 leaders—from Canada, France, Germany, Italy, Japan, Russia, UK, and the USA—welcomed the Toyako Framework for Action on Global Health¹ in their leaders' communiqué.² The document was prepared by the G8 Health Experts Group—which was convened by the Japanese Government and which met three times in the months leading up to the 2008 G8 Summit—and has now been endorsed by G8 leaders. The Framework outlines the current situation, the principles for action, and actions to be taken on global health. Although based on the language of diplomacy, thanks to the intense work done by the Japanese Government, the Framework, refreshingly, says something new and different to the usual platitudes that we have come to expect from such international summits. (...)

"HIV/AIDS: a global disaster"

Author(s):

Reference: Lancet. 05 July 2008;372(9632):2. Editorial.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673608609666/fulltext>

Published Abstract: Last week, the International Federation of Red Cross and Red Crescent Societies (IFRC) published its World Disasters Report 2008. Unlike the Federation's previous disaster reports, which have highlighted natural events, this year's report focuses on one condition—HIV/AIDS.

The report has three key messages. First, effective interventions to tackle HIV/AIDS are not being targeted at the right groups. In too many countries where the HIV epidemic is concentrated in high-risk groups (sex workers, injecting drug users, men who have sex with men), governments have taken the easy route of generalised approaches, such as school programmes. Second, money for HIV/AIDS is not flowing from donors to communities effectively. Bureaucracy, earmarked aid, and lack of coordination all mean that funds do not reach those most in need. Third, groups at high-risk of contracting HIV continue to face stigma and discrimination. Efforts to control HIV/AIDS are hampered because these groups are criminalised and have little or no access to HIV prevention and treatment services.

The IFRC is right to raise these points. 25 years after the start of the epidemic, governments should focus their HIV/AIDS programmes on those most in need, donors should ensure their aid is effective, and public-policy decisions should be based on evidence rather than moral judgments.

Why has IFRC chosen to focus on HIV/AIDS? The Federation argues that the multiple consequences of HIV/AIDS constitutes a long-term and complex disaster. In countries in southern Africa, the epidemic has had a catastrophic effect on the population, health system, economy, and social stability. HIV/AIDS is a disaster in these nations. But, even in countries with concentrated epidemics, HIV/AIDS is devastating for the marginalised groups that are left vulnerable to infection.

The IFRC believes humanitarian organisations need to increase the scale and scope of their HIV/AIDS programmes.

We agree. Visibility should not define a disaster. The HIV/AIDS epidemic deserves the increased attention of the humanitarian community.

EDITOR'S NOTE: *This article is available with a free subscription at the above website.*

"South African court bans vitamin trials for HIV/AIDS"

Author(s): Kapp C

Reference: Lancet. 05 July 2008;372(9632):15. World Report.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673608609721/fulltext>

Published Abstract:

A South African court has ruled against German-born Matthias Rath who promoted vitamins and micronutrient compounds as a cure for AIDS and claimed that antiretroviral therapy is toxic. The judgment also took the health ministry to task. Clare Kapp reports from Cape Town.

The South African Medical Association (SAMA) and Treatment Action Campaign (TAC) emerged victorious from a lengthy legal battle against a self-proclaimed vitamin guru who took advantage of health minister Manto Tshabalala-Msimang's contempt for antiretroviral (ARV) drugs to peddle his own therapies for HIV/AIDS.

Cape Town's High Court ruling on June 13 effectively ordered Matthias Rath to halt his South African operations and instructed the health minister to ensure that the order was respected.

TAC said the judgment "unequivocally establishes the duty of the state to enforce the scientific governance of medicines" and should serve as a warning to other promoters of untested and unregistered "treatments".

"Charlatans operate in every society, but they usually operate on the fringes. In South Africa, charlatanism has become mainstream...The Minister of Health has fostered this situation by creating the illusion that people with HIV have a reasonable choice to make between antiretrovirals versus alternative remedies", TAC said in a statement. South Africa has the world's highest number of people living with HIV/AIDS, with around 5.4 million of its 48 million population infected. After a slow start, the country now boasts the biggest ARV programme in the world, with 450

000 people started on to therapy by the end of February. Many health professionals say that this success is despite—rather than because of—Tshabalala-Msimang.

Rath started his operations in Cape Town around 2004, and forged a partnership with a prominent community group, the South African National Civic Organization. Rath claimed that ARVs are highly toxic and are pushed on an unsuspecting public by multinational drug cartels. In full-page newspaper adverts, leaflets, and at public meetings, he claimed that vitamins and micronutrient compounds cured HIV/AIDS. He found a receptive audience in poor townships where many people rely heavily on traditional healers and consult medical doctors as a last resort. Rath and his associates bragged about the success of a "clinical pilot study" to study the effect of vitamins and micronutrients on people presenting with AIDS symptoms.

WHO and UNAIDS condemned Rath's activities, and South Africa's Advertising Standards Association ruled that his adverts were misleading and defamatory. But the Medicines Control Council and the health department's law enforcement unit failed to take action even after the death in October, 2005, of one of Rath's patients, who appeared with him at a press conference to publicly renounce ARVs. TAC said at least five of his patients died. In November, 2005, SAMA and TAC launched their legal action against Rath and his associates—Tshabalala-Msimang and her department's director general Thami Mseleku. Cape Town's High Court Judge Dumisani Zondi banned Rath from

doing further tests. He dismissed Rath's claims that he was not doing clinical trials, saying that Rath's newspaper advertisements had declared them as such. "In my view, the Rath respondents' activity...constituted a clinical trial...Their conduct was unlawful in that they did not have permission to run clinical trials."

The judge dismissed Rath's claims that his micronutrients were nutritional supplements and said that they fell under the Medicines Control Act. He barred Rath from promoting VitaCell—the compound distributed in South Africa—pending a review by the Medicines Control Council of its medicinal claims.

The ruling also ordered the department of health to "take reasonable measures" to investigate Rath and to prevent him from doing unauthorised clinical trials and advertising the medicinal effects of VitaCell on people with HIV/AIDS.

Judge Zondi said Rath and his associates should pay 90% of the costs and Tshabalala-Msimang and Mseleku 10%.

The department of health said it would not appeal the ruling.

Even before the judgment, Rath's Cape Town operations had fizzled out. But on his website he remained unrepentant.

"The purpose of this legal attack by two ARV promoting organisations is to discredit life-saving vitamins as unwanted competition to the multi-billion business with toxic ARV drugs."

EDITOR'S NOTE: *This article is available with a free subscription at the above website.*

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10. PHARMACEUTICAL INDUSTRY

"Roche to drop HIV therapy research"

Date: 11 July 2008

Source: *Financial Times (London)*

Author(s): Andrew Jack

http://www.ft.com/cms/s/9816be18-4f79-11dd-b050-000077b07658,_i_email=y,Authorised=false.html?_i_location=http%3A%2F%2Fwww.ft.com%2Fcms%2Fs%2F0%2F9816be18-4f79-11dd-b050-000077b07658%2C_i_email%3Dy.html&_i_referer=

Roche, one of the world's largest international pharmaceuticals groups, has decided to abandon research on medicines to treat HIV in a significant blow to doctors treating the spiralling international Aids epidemic.

In a memo circulated this week to Aids specialists and activists, executives said because of disappointing results in clinical trials, the company had cancelled its programme for the compounds in development that were targeting two different ways to attack HIV.

"While we had initially been hopeful about their potential, we now have concluded that none would provide a true incremental benefit for patients compared to medicines currently on the market," said Jenny Edge-Dallas, global leader for Roche's HIV Franchise.

The move reflects Roche's strategic decision to focus only on medicines that provide a significant improvement to existing rival drugs available in the market at a time of growing demand for value for money from governments and healthcare systems.

It marks an important setback for hopes of future treatment given the constant need to develop new drugs as the rapidly rising number of existing HIV patients develop resistance to existing medicines.

Genevieve Edwards, spokesperson for the Terrence Higgins Trust, the UK-based Aids charity, said: "That's extremely disappointing news. HIV is the fastest-growing serious health condition in the UK and it remains life-threatening. One

drug absolutely does not fit all for HIV.”

While Roche, which is based in Switzerland, is not one of the largest producers of HIV medicines, it has been an important innovator in the field, launching three medicines in the past, including in 2003 Fuzeon, a “salvage” therapy, used after other drugs have failed.

The economics of the HIV market are complex in part because there are many different combinations of drugs, and much of the demand for medicines is coming from low-income countries with limited ability to pay.

Roche’s three medicines – Fuzeon, Viracept and Invirase – represented only about SFr160m (\$157m) in sales last year, giving it a far smaller share of global sales than drugs from rivals including Gilead, Bristol-Myers Squibb and GlaxoSmithKline.

The company stressed it would continue to manufacture the medicines, as well as diagnostics for HIV and other treatments for conditions with which HIV patients are often infected.

Aids research has suffered a series of blows in recent months with the failure of a series of Aids vaccines.

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11. ANNOUNCEMENTS

Sakhi Saheli - promoting gender equity and empowering young women: a training manual

http://www.popcouncil.org/pdfs/horizons/India_SakhiSaheli_Eng.pdf

The Sakhi Saheli program was adapted from Instituto Promundo's Program M by CORO and Horizons/ Population Council as part of a larger research study aimed at reducing HIV risk among young men and women by addressing gender norms. In earlier phases of the study, the Yaari Dosti program with young men was piloted and evaluated leading to the work with young women in the last phase by piloting the Sakhi Saheli program. At the start of the Sakhi Saheli program, CORO and Horizons undertook qualitative research to explore young women's construction and expression of femininity and masculinity in two urban slum communities in Mumbai. A team of peer leaders from CORO was intensively trained in data collection methods to undertake social mapping, in-depth interviews and group discussions with girls and women aged 16-24 years and key informants such as parents, community elders and teachers. The peer leaders were engaged in interpreting and analysing research findings, under the guidance of the researchers. This training manual was prepared through a two-year-long participatory process undertaken in Mumbai, India. Young women were engaged as leaders in the design and implementation of program activities, which were subsequently validated through community-based research in selected urban slum communities in India. The manual promotes critical reflection among young women, so they can recognize and understand how gender normative attitudes and behaviors affect their everyday lives and can result in increasing their vulnerability to HIV and other reproductive health problems. (excerpt)

EDITOR'S NOTE: *The full text of this document is available at the above website.*

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