



ALLIANCE FOR MICROBICIDE DEVELOPMENT

06 June 2008, Volume 9, Number 22

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/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. MONTHLY MICROBICIDE PIPELINE UPDATE

June 2008

http://www.microbicide.org/cs/microbicide_pipeline

The most recent summaries of Ongoing and Planned/Funded Clinical Trials, and Preclinical **Microbicide** Candidates are now available on the Alliance website at http://www.microbicide.org/cs/microbicide_pipeline.

Currently, there are 11 candidate products in clinical development and over 50 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.

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2. ALLIANCE UPDATES AND COMMUNITY NEWS

Direct from Delhi - Microbicides 2008 Comes to Sweet Home Chicago

<http://www.aidschicago.org/prevention/microbicides.php>

Please join the Chicago Women and Girls HIV Prevention Coalition <http://www.aidschicago.org/prevention/microbicides.php> and the International Rectal **Microbicide** Advocates for this exclusive update from across the globe on the current developments in **microbicide** research and advocacy - direct from the **Microbicides 2008** conference www.microbicides2008.com held in New Delhi, India. **Microbicides** are products currently in development that a person could use to reduce her or his risk from infection of HIV and other STDs.

Event details:

- Wednesday June 25, 2008
- 6:00-8:00 p.m.
- University Center, 525 S. State Street, Chicago, IL

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RSVP - it's FREE. <https://afc.aidschicago.org/NETCOMMUNITY/SSLPage.aspx?pid=624&srcid=183>

This dynamic event will feature **microbicide** advocacy leaders:

Latifa Boyce

Alliance for **Microbicide** Development <http://www.microbicide.org/>

Dazon Dixon Diallo

SisterLove, Inc. <http://www.sisterlove.org/>

Jim Pickett

International Rectal **Microbicide** Advocates <http://www.rectalmicrobicides.org/>

AIDS Foundation of Chicago <http://www.aidschicago.org/>

Imaging Techniques May Help Characterize Vaginal Microbicides

<http://dx.doi.org/10.1016/j.contraception.2007.11.016>

A USAID-supported study conducted by CONRAD and its partners shows that three different imaging techniques provide valuable information about the movement of a **vaginal gel** inside a woman's vagina. This information may be particularly useful in the development of a vaginal **microbicide** to prevent HIV.

Magnetic resonance imaging, gamma scintigraphy, and a fiberoptic probe were used to evaluate the movement and retention of gels inside the vagina. The scientists used two **microbicide** surrogates - Replens gel and K-Y Jelly.

The scientists showed how a woman's body movements, the number of children she has had, and her body mass index can affect the diffusion and retention of a **vaginal gel**. They also identified unique advantages and disadvantages of the imaging techniques and concluded that the three techniques would provide complementary information about a **microbicide**.

Although **microbicides** can be produced in many forms, most of the current candidates are formulated as gels. The ideal **microbicial** gel would spread quickly, completely covering both the vaginal walls and the outer part of the cervix. It would also stay in place throughout sexual intercourse. More than 30 **microbicide** candidates are in some stage of laboratory or clinical development. No product has yet been shown to prevent HIV in humans.

Family Health International provided biostatistical support to this CONRAD study. Additional partners included Duke University, Scintipharma, Inc., the University of Kentucky, and the University of Pennsylvania.

To read more about this topic, see: <http://dx.doi.org/10.1016/j.contraception.2007.11.016>.

EDITOR'S NOTE: This article abstract appeared in the 15 February 2008 issue of the Digest, available at http://www5.microbicide.org/publications/show_story.html?NewsID=2911.

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3. MEDIA COVERAGE OF MICROBICIDES

"HIV report highlights drug deficiency"

Date: 03 June 2008

Source: ABC News (Australia)

Author(s): Lindy Kerin

<http://www.abc.net.au/worldtoday/content/2008/s2263707.htm>

ELEANOR HALL: An international report on HIV-AIDS has found that the rate of new infections is increasing so fast that fewer than one third of the people who need treatment around the world are getting it.

Nearly 3 million people with the disease are now receiving life saving treatment.

But the report by the World Health Organisation, UN Aids and UNICEF warns that the supply of drugs is still not meeting demand as Lindy Kerin reports.

LINDY KERIN: The report released in Geneva overnight says significant inroads have been made in treating HIV over the past three years.

Nearly 3 million people are now receiving anti-retroviral treatment in low and middle-income countries.

That's one million more than the previous year.

But Dr Kevin De Cock the Director of the HIV-AIDS program with the World Health Organisation says despite the progress, treatment is not keeping pace with the rate of new infections.

KEVIN DE COCK: There are still about 2.5 million people becoming newly infected each year and that compares with about a million additional people coming onto treatment.

LINDY KERIN: The report found most low and middle-income countries are still far from achieving universal access to treatment.

It cites weak healthcare systems and a shortage of health professionals as the major obstacles.

Kevin De Cock says HIV-AIDS remains one of the world's greatest challenges.

KEVIN DE COCK: HIV-AIDS remains the leading infectious disease challenge in global health. This is a formidable disease to deal with as I think all of the research into vaccines for example which has not gone as well as we would have hoped has shown. This is a very complicated infection.

LINDY KERIN: There are some positive results in the report including improvements in preventing mother-to-child transmission of HIV.

At the end of last year, nearly 500,000 women had access to anti-retrovirals, that was up from 350,000 in 2006.

Bertil Lindblad is the Director of the New York Office of the UN AIDS program.

BERTIL LINDBLAD: In the last year alone you know, there were an estimated 33 per cent of all HIV positive pregnant women who could receive anti-retroviral treatment to prevent HIV transmission and that figure was 10 per cent only in 2004.

However we know that only approximately 12 per cent of pregnant women living with HIV who are identified during their ante-natal care so to speak were assessed for eligibility to receive anti-retroviral therapy.

LINDY KERIN: Experts around the globe agree that an HIV vaccine is still many years away.

Professor Tony Cunningham is the Director of the Westmead Millennium Institute and the Australian Centre for HIV and Hepatitis Virology research.

He says given the failed attempts to develop a vaccine, the roll out of anti-retroviral treatment has become even more important.

TONY CUNNINGHAM: A recent key vaccine trial conducted by Merck and various public organisations in the USA called the "STEP Trial" in which people have put a lot of health has failed and it is clear that vaccines will not be available for a long time. Some people say as long as 20 years.

In addition to that, the **microbicide** trial with cellulose sulphate using the physical properties of the candidate has also failed recently and there is a lot of concern about the potential of **microbicides** in the future.

LINDY KERIN: The UN general assembly will meet in New York next week to review the progress of HIV treatment.

Bertil Lindblad says a record number of 147 countries have submitted reports.

BERTIL LINDBLAD: What we will also discuss next week is that more needs to be done, and the message to the global community is that AIDS is a long term wave phenomenon that the world has to tackle for years to come so that is why it is so important to keep the momentum up, and also that AIDS does require exceptional message, because it's also so much more than a issue.

EDITOR'S NOTE: Further information about this report is available in the "Announcements" section of this Digest.

"Britain pledges 12 billion dollars to combat AIDS"

Date: 02 June 2008

Source: *Agence France Presse*

http://afp.google.com/article/ALeqM5ixgJcdLUUYC_uWcA5-Ne1lvJBTFg

Britain on Monday pledged six billion pounds (7.6 billion euros, 11.8 billion dollars) to improve health services and systems in developing countries in a bid to combat AIDS.

The seven-year commitment announced by International Development Secretary Douglas Alexander is in addition to one billion pounds already earmarked for the Global Fund to Fight AIDS, Tuberculosis and Malaria.

"If we are to achieve universal access, and to halt and reverse the spread of AIDS, the evidence demonstrates that we require a long-term approach, across a range of health systems and services," Alexander said in a written statement to the House of Commons.

He said the six-billion-pound commitment "demonstrates (Britain)'s determination to remain at the forefront of global efforts to achieve universal access."

As part of the government's new strategy, it will work with others to lower the cost of treatment, and increase the coverage of services for injecting drug users.

It also aims to help support orphans and vulnerable children, particularly those affected by AIDS, and increase the availability of family planning information and condoms.

According to Alexander, Britain will also ramp up by at least 50 percent its funding for research into AIDS vaccines and **microbicides**, substance compounds that can be applied inside a vagine or rectum to prevent the spread of sexually-transmitted diseases.

Effective **microbicides** are not yet available, according to the World Health Organisation.

The announcement was welcomed by British charity Oxfam, which cautioned, however, that more needed to be done.

"The announcement of this much-needed, long-term financial commitment to help strengthen health systems in the developing world is a very welcome one," said Phil Bloomer, the charity's director of campaigns and policy.

"But tackling the AIDS epidemic will require more than investment in health systems. It is also about factors such as education, awareness-raising, counselling, and the provision of security of food and income for all those who need it, whether infected or affected."

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4. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

"Biological and technical variables affecting immunoassay recovery of cytokines from human serum and simulated vaginal fluid: a multicenter study"

Author(s): Fichorova RN, Richardson-Harman N, Alfano M, et al

Reference: N/A Epub ahead of print.

<http://pubs.acs.org/cgi-bin/abstract.cgi/ancham/asap/abs/ac702628q.html>

Published Abstract: The increase of proinflammatory cytokines in vaginal secretions may serve as a surrogate marker of unwanted inflammatory reaction to **microbicide** products topically applied for the prevention of sexually

transmitted diseases, including HIV-1. Interleukin (IL)-1 β and IL-6 have been proposed as indicators of inflammation and increased risk of HIV-1 transmission; however, the lack of information regarding detection platforms optimal for vaginal fluids and interlaboratory variation limit their use for **microbicide** evaluation and other clinical applications. This study examines fluid matrix variants relevant to vaginal sampling techniques and proposes a model for interlaboratory comparisons across current cytokine detection technologies. IL-1 β and IL-6 standards were measured by 12 laboratories in four countries, using 14 immunoassays and four detection platforms based on absorbance, chemiluminescence, electrochemiluminescence, and fluorescence. International reference preparations of cytokines with defined biological activity were spiked into (1) a defined medium simulating the composition of human vaginal fluid at pH 4.5 and 7.2, (2) physiologic salt solutions (phosphate-buffered saline and saline) commonly used for vaginal lavage sampling in clinical studies of cytokines, and (3) human blood serum. Assays were assessed for reproducibility, linearity, accuracy, and significantly detectable fold difference in cytokine level. Factors with significant impact on cytokine recovery were determined by Kruskal-Wallis analysis of variance with Dunn's multiple comparison test and multiple regression models. All assays showed acceptable intra-assay reproducibility; however, most were associated with significant interlaboratory variation. The smallest reliably detectable cytokine differences ($P < 0.05$) derived from pooled interlaboratory data varied from 1.5- to 26-fold depending on assay, cytokine, and matrix type. IL-6 but not IL-1 β determinations were lower in both saline and phosphate-buffered saline as compared to vaginal fluid matrix, with no significant effect of pH. The (electro)chemiluminescence-based assays were most discriminative and consistently detected <2 -fold differences within each matrix type. The Luminex-based assays were less discriminative with lower reproducibility between laboratories. These results suggest the need for uniform vaginal sampling techniques and a better understanding of immunoassay platform differences and cross-validation before the biological significance of cytokine variations can be validated in clinical trials. This investigation provides the first standardized analytic approach for assessing differences in mucosal cytokine levels and may improve strategies for monitoring immune responses at the vaginal mucosal interface.

EDITOR'S NOTE: Some characters in this abstract may not appear correctly in the PDF version of the Digest. Please view the web-based version or the original article to see the correct characters.

"Phase I clinical trial of repeat dose terameprocol vaginal ointment in healthy female volunteers"

Author(s): Khanna N, Dalby R, Connor A, et al

Reference: N/A 35(6):577-82.

<http://www.stdjournal.com/pt/re/std/abstract.00007435-90000000-99530.htm;jsessionid=LGPgcq2xGDxkqD8TGH1BpQxriQJfyDZwnTvzhy6WNnnyh6LnZXVJ!634347399!181195628!8091!-1?index=1&database=ppvovft&results=1&count=10&searchid=1&nav=search>

Published Abstract: Objectives: This safety study of terameprocol (also called M4N, EM-1421) daily vaginal application in healthy women explores its potential application as a **microbicide** in interrupting human immunodeficiency virus sexual transmission and additional interruption of human papillomavirus and herpes simplex virus transmission. Methods: A double-blind placebo controlled phase I repeat dose tolerability and pharmacokinetic, crossover study of 90 mg terameprocol (2% w/w ointment) administered intravaginally for 7 consecutive days in healthy female subjects. The pharmacokinetics after administration was examined on days 1 and 7 of dosing.

Subjects underwent vaginal examination following the 6-hour pharmacokinetic sample on day 7 of each study period. Results: Recruitment started January 2006 and ended May 2006, and 14 subjects completed the study. Median age was 24 years. No treatment-related serious adverse events were reported, and there were a total of 17 treatment-emergent adverse events (AE) reported by 11 participants. The most common AE was headache. Terameprocol was not detectable in serum in pharmacokinetic samples. Conclusions: Terameprocol was well tolerated at a 90 mg dose (2% wt/wt) administered vaginally daily for 7 days. No serious adverse events occurred and any AEs were mild. The excellent safety profile supports future clinical trial to evaluate the application of intravaginal terameprocol in women.

"Topical oestrogen keratinises the human foreskin and may help prevent HIV infection"

Author(s): Pask AJ, McInnes KJ, Webb DR, et al

Reference: N/A 3(6):e2308.

<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0002308>

Published Abstract: With the growing incidence of HIV, there is a desperate need to develop simple, cheap and effective new ways of preventing HIV infection. Male circumcision reduces the risk of infection by about 60%, probably because of the removal of the Langerhans cells which are abundant in the inner foreskin and are the primary route by which HIV enters the penis. Langerhans cells form a vital part of the body's natural defence against HIV and only cause infection when they are exposed to high levels of HIV virions. Rather than removing this natural defence mechanism by circumcision, it may be better to enhance it by thickening the layer of keratin overlying the Langerhans cells, thereby reducing the viral load to which they are exposed. We have investigated the ability of topically administered oestrogen to induce keratinization of the epithelium of the inner foreskin. Histochemically, the whole of the foreskin is richly supplied with oestrogen receptors. The epithelium of the inner foreskin, like the vagina, responds within 24 hours to the topical administration of oestriol by keratinization, and the response persists for at least 5 days after the cessation of the treatment. Oestriol, a cheap, readily available natural oestrogen metabolite, rapidly keratinizes the inner foreskin, the site of HIV entry into the penis. This thickening of the overlying protective layer of keratin should reduce the exposure of the underlying Langerhans cells to HIV virions. This simple treatment could become an adjunct or alternative to surgical circumcision for reducing the incidence of HIV infection in men.

EDITOR'S NOTE: *The full text of this article is available for public access at the above website. A media write-up of this article is available at http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=52544. An interview with the researchers is available at <http://www.abc.net.au/pm/content/2008/s2265320.htm>.*

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5. PUBLISHED RESEARCH: RELEVANT BASIC AND TRANSLATIONAL SCIENCE

"Bacterial vaginosis and vaginal yeast, but not vaginal cleansing, increase HIV-1 acquisition in African women"

Author(s): van de Wijgert JH, Morrison CS, Cornelisse PG, et al

Reference: N/A 48(2):203-210.

<http://www.jaids.org/pt/re/jaids/abstract.00126334-200806010-00013.htm;jsessionid=LD5GQZjCJcSSGh2TK0JHn39HpjbNPNhwLWrJRggDMJjJ91qvh93p!634347399!181195628!8091!-1>

Published Abstract: Objective: To evaluate interrelationships between bacterial vaginosis (BV), vaginal yeast, vaginal practices (cleansing and drying/tightening), mucosal inflammation, and HIV acquisition. Methods: A multicenter, prospective, observational cohort study was conducted, enrolling 4531 HIV-negative women aged 18 to 35 years attending family planning clinics in Zimbabwe and Uganda. Participants were tested for HIV and reproductive tract infections and were interviewed about vaginal practices every 3 months for 15 to 24 months. BV was measured by Gram stain Nugent scoring, vaginal yeast by wet mount, and mucosal inflammation by white blood cells on Gram stain. Results: HIV incidence was 4.12 and 1.53 per 100 woman-years of follow-up in Zimbabwe and Uganda, respectively (a total of 213 incident infections). Women with BV or vaginal yeast were more likely to acquire HIV, especially if the condition was present at the same visit as the new HIV infection and the visit preceding it (hazard ratio [HR] = 2.50, 95% confidence interval [CI]: 1.68 to 3.72 and HR = 2.97, 95% CI: 1.67 to 5.28 for BV and yeast, respectively). These relationships did not seem to be mediated by mucosal inflammation. Vaginal drying/tightening was associated with HIV acquisition in univariate (HR = 1.49, 95% CI: 1.03 to 2.15) but not multivariate models. Vaginal cleansing was not associated with HIV acquisition. Conclusions: BV and yeast may contribute more to the HIV epidemic than previously thought.

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6. HIV/AIDS VACCINES

"HIV vaccine trial to have substantial design changes"

Date: 02 June 2008

Source: *Medical Device Daily*

Author(s): Bob Roehr

<http://www.medscape.com/viewarticle/575458>

Discussions at last week's National Institute of AIDS and Infectious Diseases (NIAID) AIDS Vaccine Research Subcommittee (AVRS) meeting may have substantial implications for the next HIV vaccine trial, on hold since last fall. It is likely to move forward with substantial changes in the scientific questions asked, the endpoints measured, and the number and type of participants.

The Partnership for AIDS Vaccine Evaluation (PAVE) 100 trial as initially conceived was an ambitious phase 2b trial of about 8500 participants in 13 countries on 3 continents. Using a DNA prime made up of 6 plasmid constructs (gag, pol, and nef, plus env from clade A, B, and C virus), patients would receive 3 injections (at baseline, 1, and 2 months)

followed by an adenovirus vector 5 (Ad5) booster at 6 months. The product was developed by the NIAID Vaccine Research Center (VRC).

But in September 2007, investigators learned that more participants in Merck's phase 2b STEP vaccine trial were becoming infected with HIV than were those who had received the placebo. Nor was there any evidence of support in the secondary endpoint, an immune response that resulted in a lower viral load set point that might slow the course of disease progression. That trial was stopped and all other vaccine trials were placed on hold until researchers could figure out why.

Two factors emerged as associated with higher risk for infection in subsequent analysis: one was being uncircumcised, the other was higher titers of antibody to Ad5 from previous natural exposure to the virus. The former presumably increased the risk of HIV acquisition through sexual activity while the latter resulted in a blunted response to the vaccine.

A central question became whether the PAVE 100 trial was sufficiently different from STEP for it to move forward. At an AVRS meeting in December, supporters made the case that it was, but the committee wanted to see further post-hoc analysis of the STEP trial, particularly analysis of immune function generated by both vaccines as measured by the same assays. Prior studies had been conducted using different assays and methodologies, making head-to-head comparisons difficult.

What's New

At last week's committee meeting, M. Juliana McElrath, MD, PhD, from the University of Washington in Seattle, presented an impressive amount of new data and analysis that the AVRS had requested. It showed that the 2 vaccines generated somewhat different immune responses, as would be expected given the somewhat different constructs used in each. STEP generated stronger responses in some areas, and PAVE in others. Analysis of proliferation and neutralization remains to be performed.

Those differences may have been statistically significant in some instances, but there was little reason to believe that they might be clinically significant. There are no established correlates of protection in humans, but animals that naturally control SIV infection exhibit an immune response that is many times broader in terms of the number of epitopes recognized, and the immune response was of greater magnitude than either of the vaccines generated in humans.

Dr. McElrath did point out that a few vaccinated individuals in the STEP trial appeared to have an association between a higher response to gag and a lower viral set point. The analysis was post hoc and offered a clue as to where future investigation might focus.

PAVE Revamped

The PAVE 100 sponsors substantially revised the trial in light of issues raised by the STEP trial and recommendations by the AVRS. Principal investigator Scott Hammer, MD, professor of medicine at Columbia University in New York City, presented the current iteration. The product and its administration would remain the same, but the study population would be greatly restricted, they would be studied much more intensely, and the emphasis would shift from product development toward basic research.

The study would shrink to 2400 participants; the international groups would disappear; and enrollees would be exclusively men who have sex with men (MSM) who are both circumcised and have no measurable antibodies to Ad5 at screening. It assumes a 3% incidence of HIV infection within the study population, a conservative projection given the 4.6% incidence that actually occurred in a similar population in the STEP trial.

The new primary endpoints are (1) effect on viral set point among those who become infected and (2) safety of the product. The secondary objectives are to determine:

- efficacy at preventing infection
- predictive value of early specific CD8+ T-cell response to a lower viral set point or protection from infection
- immunogenicity of the product
- effect on disease progression

Additional study of viral isolates and immune response will may enable a better understanding of the basic science of early infection and development of better tools to measure response.

Community Perspective

Several community advocacy organizations in their oral and written testimony focused on how the revised PAVE 100 differs from a traditional vaccine trial. The revisions will require a substantial educational effort to ensure informed consent from those participating in it.

Martin Delaney with Project Inform was not convinced that trial should move forward. He called the data "singularly unconvincing." After hearing the comparative analysis presented for the first time, he concluded, "There was really no pattern of superiority, only patterns of differences. That is a word of caution as to whether these vaccines are really different."

He added, "We are asking so little in this trial. It is not going to protect people, it very likely is not going to affect viral load. And if it fails to meet even those endpoints, it is going to have a very hard time with the media and in Congress 3 years from now."

Mr. Delaney reminded the group, "The goal is not to create an HIV vaccine, the goal is to bring the HIV epidemic under control. A vaccine is a way to do that, but it is not the only way to do it, it is just one of them."

The Treatment Action Group (TAG) said in a submitted statement, "Based on the information that is currently available to us, we feel that the uncertainties argue against spending human and fiscal resources on PAVE 100 and instead suggest focusing on improving T cell-based immunogens so they can be studied in a broader population with a greater chance of success."

Skeptics Ask for Delay

NIAID's Anthony Fauci, MD, PhD, posed the central question for the advisory committee: "Is there a reasonable chance that the field will gain from this in a way that is really discovery, as opposed to developing a product?"

The greatest reservations came from those working most closely with nonhuman primates. The University of Wisconsin's David Watkins, PhD, pointed out that the challenge in animals is autologous to the vaccine constructs, while the natural challenge to humans likely will be heterologous.

He added, "We need to remember that the number of epitopes induced by DNA/Ad in macaques far exceeds the 2 or 3 epitopes induced in humans. I have a hard time using the nonhuman primate data to support moving forward with this particular vaccine."

Bruce Walker, MD, from the Partners AIDS Research Center, thought the STEP and PAVE vaccines "are essentially indistinguishable." He saw little reason to proceed with the trial as a protective vaccine but did support it as a study to better understand vaccine-induced immune responses and perhaps identify correlates. But the study needs to be framed and explained to participants in those terms, he said.

Dennis R. Burton, PhD, from Scripps Research Institute, confessed to going back and forth as to whether the trial should proceed. He did not believe it to be a trial so much as "a human experiment." He suggested that in the lab, such an experiment would not move forward without greater rigor. "I'd be more in favor of taking a step back and thinking about what it is that we want to know from this experiment, and making sure that we have everything in place to do that."

Cornell University researcher John Moore, PhD, shared those concerns. "We have to define what we are going to learn and how we are going to learn it." He urged inclusion of a component on host genetics and correlates of immunogenicity.

Supporters Encourage Moving Forward

Jerald C. Sadoff, MD, president of the Aeras Global TB Vaccine Foundation, was perhaps the most upbeat person on the panel. He saw the events as "a normal part of vaccine development" where failure is standard. He reminded the committee that a vaccine for malaria grew from identifying protection in a single individual and amplifying that into broader coverage and protection through the iterative process.

He focused on the weak inverse correlation between viral load and cellular immune responses that was found in the retrospective analysis. "It is the only positive finding of vaccine-induced protection in the entire field of HIV vaccine research. There is not another example in humans of such a finding, whether it is valid or not. There is no way to make it valid except to repeat it," Dr. Sadoff stressed.

"In my mind, the purpose of this experiment is to repeat that and find out if it is true. Everything else is gravy." From that perspective, Dr. Sadoff worried that the 2 vaccines might not be similar enough.

Lawrence Corey, MD, a researcher at the University of Washington in Seattle and principal investigator of the HIV Vaccine Trials Network (HVTN), argued that PAVE was necessary to establish whether the STEP trial was a failure of a product or of the T-cell vaccine concept in influencing acquisition and disease progression.

He downplayed the impact of another potential failure because that is several years away and the public can absorb it over time. Dr. Corey added that delay will only increase the size and cost of a trial because preexposure prophylaxis (PrEP) trials are likely to begin enrolling participants in 18 to 24 months. New, refined assays are most likely to be developed within the context of an ongoing trial.

"STEP was a landmark trial that wakened up from this blissful state of optimism of where we were in the vaccine field," Dr. Corey said. He said he thinks the field needed "the reality test" of other trials to move forward.

Susan Buchbinder, MD, from the San Francisco Department of Health, pointed to the 4.6% incidence of infection within the MSM participants in the STEP trial as a reason to proceed, particularly within the new target population of the PAVE trial.

Some questioned how using an Ad5 vector in persons who had not been previously exposed to that virus might be transferable to the broader world stage where levels of antibody to Ad5 are more common and higher than what is seen in the United States.

But the Gates Foundation's Margaret A. Liu, MD, saw this as "broadening the possible relevance of the results rather than narrowing it, because it is much more similar to [what would be seen with other vectors in development] where people do not have preexisting immunity."

Fauci's Dilemma

Dr. Fauci has devoted an inordinate and intense amount of time to questions surrounding HIV vaccine development. In closing remarks he said we are in "a spectacularly unique position [in terms of] how little we know." We don't even know if immune protection is possible, he said.

In speaking with reporters he thought there was a broad consensus to move forward with the trial. He acknowledged that there may be additional minor modifications to the PAVE 100 protocol, and that outright cancellation would result in few net savings given the fixed costs already invested in the trial.

Dr. Fauci said he anticipates a fairly quick decision on whether the modified PAVE trial will move forward.

EDITOR'S NOTE: A subscription is required to view this article at its original location.

"A STEP into darkness or light?"

Source: *Science*. 2008 May 16;320(5878):849. Editorial.

Author(s): John P Moore, PJ Klasse, Matthew J Dolan, et al

<http://www.sciencemag.org/cgi/content/summary/320/5877/753>

The outcome of the efficacy trial of an adenovirus serotype 5 (Ad5) vectorbased HIV-1 vaccine last November (STEP trial) was unexpected. Not only was the vaccine ineffective at lowering plasma viremia postinfection, but it may have increased the risk of acquiring HIV-1 infection. Although firm conclusions cannot be drawn based on the small number of infections that occurred (49 in the vaccinated patient group, 33 in the placebo group), it has been suggested that vaccineinduced generalized immune activation, which can promote HIV-1 replication, might have increased the infection risk (1).

The vector-based vaccine used in the STEP trial was a recombinant Ad5 virus expressing immunogenic HIV-1 proteins. A higher number of HIV-1 infections occurred in the subset of vaccinees with high, preexisting titers of Ad5-specific antibodies, compared with placebo recipients. One possible explanation is that anti-Ad5 antibodies facilitate cellular uptake of the Ad5 vector (perhaps by cells other than the ones normally targeted), inducing an immune response that enhances HIV-1 infection. Although immune responses to viral infections are usually protective, they can also be harmful (as with West Nile, dengue, measles, and respiratory syncytial virus infections). For example, a low-titer antibody response to West Nile virus can enhance viral replication and exacerbate disease (2). Whether similar events occur after vaccination with an Ad5 or similar viral vector is now something to consider.

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

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7. OTHER PREVENTION APPROACHES

"Women: Men must be encouraged to practise safe sex too"

Date: 02 June 2008

Source: *The Star (Malaysia)*

<http://thestar.com.my/news/story.asp?file=/2008/6/2/nation/21425673&sec=nation>

Women's groups have come out in support of the Health Ministry for promoting the use of condoms to combat HIV, but say practising safe sex is the responsibility of both men and women.

Sisters in Islam programme manager Norhayati Kaprawi said it was her group's hope that both men and women are encouraged to practise safe sex.

"We hope the ministry allocates a bigger budget for free condoms for those who need it, like drug abusers and their partners."

Norhayati said the Government should also introduce sex education in schools.

She was responding to the call by Deputy Health Minister Datuk Dr Abdul Latiff Ahmad for every woman to carry a condom for her own protection.

Women's Aid Organisation executive director Ivy Josiah said it should be a joint responsibility.

"I am glad that he brought up the issue. However, our view is that we should be educating men to use condoms.

"Many women find it difficult to negotiate with their partners that they should use a condom, especially for women who are in partnerships where there is violence or control."

In her blog, former Malaysian AIDS Council chairman Datin Paduka Marina Mahathir concurred that men have to play their part too in practising safe sex.

"It is one thing to carry condoms, it's quite another thing to get the guy to use them. It might be more useful to tell men to carry condoms instead," she said.

She also said that the police should not assume women who possess condoms were soliciting for sex.

"The issue is that having a condom in one's handbag is often used as evidence by the police that one is soliciting (which is a crime).

"Thus, unless we're supposed to all carry letters from Dr Latiff saying "it's okay," women carrying condoms can be arrested for soliciting for clients to provide sexual services. In other words, it will be assumed that they are sex workers," she said.

"Uganda: Condom stocks run low"

Date: 31 May 2008

Source: *New Vision*

Author(s): Charles Odongtho

<http://allafrica.com/stories/200806021200.html>

Unless the procurement process is fast-tracked, Uganda could have no condoms in October. A United Nations Population Fund (UNFPA) official sounded the warning during a press briefing in Kampala on Friday.

"We projected 80 million condoms would last till the end this year, but considering the current consumption of eight million per month with no new orders made, we will not have any left by October," said programme associate Brian Kironde.

UNFPA, together with the United States Agency for International Development, are the main suppliers of condoms in the country. Uganda consumes about 130 million condoms annually.

"Four in five Swazi men reject AIDS testing: survey"

Date: 30 May 2008

Source: *Agence France Presse*

http://news.yahoo.com/s/afp/20080530/hl_afp/swazilandhealthaids

Four out of five men in Swaziland, the nation with the world's highest rate of HIV, would refuse to undertake a test for the AIDS virus, official figures showed on Friday.

A total 79.6 percent of those questioned in a survey said they would not be willing to take a test while only a minority (46 percent) said they were prepared to use condoms, the central statistics office said.

The same survey further revealed that 40 percent of Swazi men believed that spousal abuse could be justified under certain circumstances.

Close to 40 percent of adults in the landlocked southern African nation are living with HIV and AIDS, the highest infection rate anywhere in the world, according to UN figures.

In a report released last year, the Physicians for Human Rights organisation said that a cultural belief that women are inferior to men had helped spur the rapid spread of HIV in Swaziland, Africa's last absolute monarchy.

The current monarch, King Mswati III, has 13 wives.

"The safety of adult male circumcision in HIV-infected and uninfected men in Rakai, Uganda"

Author(s): Kigozi G, Gray RH, Wawer MJ, et al

Reference: N/A 5(6):e116.

<http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0050116>

Published Abstract: *Background* The objective of the study was to compare rates of adverse events (AEs) related to male circumcision (MC) in HIV-positive and HIV-negative men in order to provide guidance for MC programs that may provide services to HIV-infected and uninfected men. *Methods and Findings* A total of 2,326 HIV-negative and 420 HIV-positive men (World Health Organization [WHO] stage I or II and CD4 counts greater than 350 cells/mm³) were circumcised in two separate but procedurally identical trials of MC for HIV and/or sexually transmitted infection prevention in rural Rakai, Uganda. Participants were followed at 1-2 d and 5-9 d, and at 4-6 wk, to assess surgery-related AEs, wound healing, and resumption of intercourse. AE risks and wound healing were compared in HIV-positive and HIV-negative men. Adjusted odds ratios (AdjORs) were estimated by multiple logistic regression, adjusting for baseline characteristics and postoperative resumption of sex. At enrollment, HIV-positive men were older, more likely to be married, reported more sexual partners, less condom use, and higher rates of sexually transmitted disease symptoms than HIV-negative men. Risks of moderate or severe AEs were 3.1/100 and 3.5/100 in HIV-positive and HIV-negative participants, respectively (AdjOR 0.91, 95% confidence interval [CI] 0.47-1.74). Infections were the most common AEs (2.6/100 in HIV-positive versus 3.0/100 in HIV-negative men). Risks of other complications were similar in the two groups. The proportion with completed healing by 6 wk postsurgery was 92.7% in HIV-positive men and 95.8% in HIV-negative men ($p = 0.007$). AEs were more common in men who resumed intercourse before wound healing compared to those who waited (AdjOR 1.56, 95% CI 1.05-2.33). *Conclusions* Overall, the safety of MC was comparable in asymptomatic HIV-positive and HIV-negative men, although healing was somewhat slower among the HIV infected. All men should be strongly counseled to refrain from intercourse until full wound healing is achieved.

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

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8. POLITICS AND POLICY

"FDA changes rules for clinical trials outside the US"

Date: 04 June 2008

Source: AAAS Policy Alert

The FDA recently rejected the requirement that data from clinical trials conducted outside the United States could only be used in approval decisions if the trials adhere to the 1989 version of the Declaration of Helsinki, issued by the World Medical Association. Instead, starting in October, there will be a requirement that the studies follow "good clinical practice," which includes oversight by an independent ethics committee and informed consent provisions. This means that the approval of new drugs in the United States can be based on international drug trials that only incorporate a placebo control rather than giving all subjects access to current standards of care. It has raised concerns that the ruling will result in more "outsourcing" of clinical trials and could have negative impacts on populations from the developing world who participate in trials.

EDITOR'S NOTE: Further information about this change is available at

<http://www.regulations.gov/fdmspublic/component/main?main=DocumentDetail&o=0900006480537f08>

"Global Challenges: Speakers at second HIV/AIDS implementers' meeting in Uganda call for increased HIV prevention efforts"

Date: 04 June 2008

Source: Kaiser Daily HIV/AIDS Report

http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=52511

Conference delegates on Tuesday at the opening of the 2008 HIV/AIDS Implementers' Meeting in Kampala, Uganda, called on countries to increase HIV prevention methods in order to fight complacency about the disease, Xinhuanet reports. Some HIV/AIDS experts speaking at the conference said that although countries have started recording lower HIV/AIDS rates, most responses do not pay enough attention to prevention.

UNAIDS Executive Director Peter Piot said that although "87% of countries in the world have established clear and ambitious goals for HIV treatment, only about 50% have targets for HIV prevention therapy." He added, "There is no room for complacency. AIDS is not done; the epidemic is not under control. For every two persons who are put on treatment, five are infected" with HIV.

Ugandan President Yoweri Museveni, who opened the conference, attributed the complacency about the disease to the provision of antiretroviral treatment, which some people view as a cure for the disease. He said that HIV/AIDS messages should be repackaged, adding that he does not want to give people living with the disease "false security" that antiretroviral drugs are a cure. Mark Dybul, U.S. Global AIDS coordinator who administers the President's Emergency Plan for AIDS Relief, added that countries should take HIV prevention as seriously as HIV/AIDS treatment (Xinhuanet, 6/4).

This year's conference -- which has the theme "Scaling Up Through Partnerships: Overcoming Obstacles to Implementation" -- aims to share lessons learned in the fight against HIV/AIDS with a focus on increasing prevention, treatment and care. The conference also aims to build local capacity and bolster coordination between partners. Participants will focus on several issues, including human capacity development, connecting people with resources, coordination, integrating services, and the impact of monitoring and evaluation. In addition, the conference will focus on developing future directions for HIV/AIDS programs by focusing on implementation, identifying barriers and integrating best practices (Kaiser Daily HIV/AIDS Report, 6/3).

Archived webcasts from the meeting will be available online at www.kaisernetwork.org.

"Study throws doubt over China's clinical trial quality"

Date: 02 June 2008

Source: *in-Pharma Technologist.com*

Author(s): Kirsty Barnes

<http://www.in-pharmatechnologist.com/news/ng.asp?n=85618&c=W1FT1f7k%2BpK%2FZ1XbyFB%2BZw%3D%3D>

As China's contract clinical trials industry heats up, a new study casts doubt over the quality of the research being conducted in the country.

Researchers from the Department of Public Health and Epidemiology and the Department of Primary Care and General Practice at the University of Birmingham, UK, as well as the Institute of Respiratory Diseases, Guangzhou Medical College, China, concluded that "reporting of randomised controlled trials (RCTs) in China requires substantial improvement to meet the targets of the CONSORT statement".

Consolidated Standards of Reporting Trials (CONSORT) is a set of international guidelines pertaining to the conduct and the reporting of RCTs. It includes recommended items designed to report the methodology and conduct of a study that are common to many standard quality assessment checklists.

"The conduct of Chinese RCTs cannot be directly inferred from the standard of reporting; however without good reporting the methods of the trials cannot be clearly ascertained," the researchers added.

These conclusions were drawn after a systematic review of RCTs conducted in China and published in 2004, to ascertain their characteristics, assess the quality of their reporting, and the quality of their conduct.

It was found that out of 307 RCTs that were analysed, 199 (65 per cent) failed to report methods of randomisation and 254 (82 per cent) did not mention blinding of either participants or investigators.

"Reporting of baseline characteristics, primary outcome and length of follow-up was inadequate in a substantial proportion of studies," researchers wrote, citing the fact that less than 11 per cent of RCTs mentioned ethical approval and only 18 per cent "adequately discussed" informed consent.

However, they did point out that on a positive note, dropout rates were very "favourable" with nearly 44 per cent of trials reporting a zero dropout rate.

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

"Exploiting a research underclass in Phase 1 clinical trials"

Source: *N Engl J Med.* 2008 May 29;358(22):2316-17. *Perspective.*

Author(s): Carl Elliott, Roberto Abadie

<http://content.nejm.org/cgi/content/full/358/22/2316?query=TOC>

In November 1996, the Wall Street Journal reported that Eli Lilly was paying homeless alcoholics from a local shelter to participate in safety testing of new drugs at its trial site in Indianapolis.¹ "These individuals want to help society," asserted Lilly's director of clinical pharmacology. The subjects, however, said they took part for easy money and free room and board. Although Lilly reportedly offered the lowest per diem in the business, it managed to attract poor subjects from all over the country.¹ The medical director of the local Homeless Initiative Program said Lilly had created a "shadow economy" of paid human subjects.

Today, the Lilly episode seems like an early warning about an emerging set of ethical problems. Over the past decade, clinical trials have moved from universities to private testing sites, the pressure to recruit subjects quickly has intensified, and ethical oversight has been outsourced to for-profit institutional review boards (IRBs). Payment to subjects has escalated, creating "shadow economies" in cities throughout North America and elsewhere. In 2005, Bloomberg Markets reported that SFBC International, a contract research organization, was paying immigrants to participate in drug trials under ethically questionable conditions in a dilapidated Miami motel. A few months later, nine apparently previously healthy subjects at an SFBC subsidiary in Montreal contracted latent tuberculosis during a trial of an immunosuppressant. In 2006, six healthy subjects required intensive care in a phase 1 trial of a monoclonal antibody at a London facility run by the contract research organization Parexel. For all the ethical debate over these cases, however, few commentators have addressed the most troubling question: Is it ethically problematic to pay poor people to test the safety of new drugs?

Paying study subjects is not a new practice, but neither is it uncontroversial. According to regulators, payment should not be so high as to become an "undue inducement," lest subjects enroll in risky, unpleasant, or degrading trials against their better judgment. But this standard gives IRBs little practical guidance: a sum of money that the wealthy can easily resist may be very tempting for poorer people. Keeping payments low, however, seems unfair to the poor, who submit to trials precisely because they need the money. And whether or not such people are being unduly induced, the larger question is whether they are being exploited.

To exploit people is to take unfair advantage of them, but there is no consensus that current trial arrangements are unfair. Defenders of the status quo argue that people who enroll in trials have agreed to their conditions, that they get paid enough to make it worth their while, and that they are made better off by the arrangement. Nevertheless, there

are good reasons to believe that poor subjects are being exploited.

First, poor people are less likely than wealthier ones to get access to the drugs in question, if and when they are approved. Volunteers are unlikely to have full-time employment or, therefore, to have health insurance. Placing the burden of safety testing on the poor appears to contravene article 19 of the Declaration of Helsinki, which states that medical research is ethically justified only if there is a reasonable chance that the population in which it is conducted will benefit from the results.

Second, the U.S. oversight system is not well equipped to monitor a highly competitive, market-based, multinational research industry. The Office for Human Research Protections has no jurisdiction over privately sponsored studies, and the Food and Drug Administration inspects only about 1% of clinical trials.² IRBs, the most important bodies charged with protecting subjects, were designed primarily to review trial design, risk-benefit ratios, and informed-consent documents. Recent research scandals - which have been uncovered largely by investigative reporters rather than regulators - have concerned a very different set of issues: fraud, conflicts of interest, unfair payment practices, and unsafe or degrading trial conditions. Such problems are magnified still further when studies are conducted at private testing sites and reviewed by for-profit IRBs that are financially dependent on research sponsors.

Third, even though the purpose of phase 1 trials is to test whether new drugs are safe, most sponsors apparently do not provide free care or treatment for subjects who are injured in these trials. In fact, no agency is even tracking injuries in phase 1 trials, much less the long-term health of people who volunteer for many trials over a period of years. A recent study commissioned by the Department of Health and Human Services showed that only 16% of academic health centers provide injured subjects with free care. None compensate injured subjects for pain and suffering or lost wages.³ Although no comparable data are available for private research sponsors, there is little reason to believe that private sponsors are much more generous⁴; indeed, many include disclaimers in their consent forms indicating that subjects retain responsibility for their own medical care.

Most of these problems can be seen as consequences of the transformation of clinical research into a business. Many subjects in phase 1 trials today see their participation as a job.⁵ They must pay taxes on their trial income, and sponsors often require them to sign a form acknowledging their status as "independent contractors." The payment has become high enough to make participating in trials more lucrative than holding a minimum-wage job, even if subjects abide by the requirement that they wait 30 days between trials. Yet subjects get none of the rights or benefits that come with a good job, such as workers' compensation, the right to unionize, disability benefits, or health insurance. Subjects whose livelihoods depend on trial income are often reluctant to drop out of trials that turn out to be risky or unpleasant, especially if they have traveled some distance to the trial site and have invested a substantial amount of money in accommodations while waiting to enter the trial. Subjects have little incentive to be truthful about their medical history or health status because known medical problems may preclude their participation in a study. Nor do they have anyone to go to with complaints. Many say they are reluctant to complain to sponsors about poor conditions for fear of being excluded from future trials. For similar reasons, they are reluctant to go to a lawyer, even if a trial goes seriously wrong.⁴

Without actually intending to do so, policymakers have allowed participation in clinical trials to become something very close to a job. Sponsors call subjects' payments "compensation" to suggest that they are merely reimbursing participants for expenses and inconvenience, even as they fill studies with unemployed people who depend on trial income to make ends meet. They refer to paid subjects as "volunteers," implying that participation is a freely chosen

act of altruism, whereas most subjects indicate that they take part in trials for the money. Regulators allow sponsors to use money to attract subjects but do not require them to provide the kinds of benefits that subjects would demand if they had more power. The result is what one Philadelphia trial subject describes as "a mild torture economy." "You are not being paid to do something," he explains. "You are being paid to endure."⁵

EDITOR'S NOTE: This article, including references, is available for public access at the above website.

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9. HIV/AIDS FUNDING

"Institute gets \$20 million grant to transition research to marketplace"

Date: 29 May 2008

Source: *San Diego Union-Tribune*

Author(s): Keith Darce

<http://www.signonsandiego.com/news/business/20080529-1838-bn29scripps2.html>

The Scripps Translational Science Institute in La Jolla received a \$20 million, five-year grant Thursday. The award propelled the institute - founded last year - into an expanding group of federally funded research centers focused on turning laboratory findings into treatments for patients.

Institute officials described the grant, by the National Institutes of Health, as a major milestone. They said it will jumpstart a diverse body of research ranging from genetic sequencing to community diabetes programs.

"This puts (us) on the map. This award validates our work in this area," said Chris Van Gorder, president and CEO of Scripps Health, which co-founded the translational center along with The Scripps Research Institute.

The grant also could help the center attract more funding from government and private sources, said Joe Panetta, president and CEO of BioCom, the biotechnology industry's trade group in Southern California.

"Because this money can be used to get the foundations of a translational research program laid out, it then can be (used) to show the promise for future work that can be done," he said.

The center, created in January 2007, is located on the campus of The Scripps Research Institute. Eight research organizations, most of them in San Diego County, collaborate with it.

Thursday's award nearly doubles the total budget for the center, which is directed by noted cardiologist and genetics researcher Eric Topol.

It is part of the Clinical Translation Science Award, which federal officials created in 2006 to reduce the time it takes for research findings to become actual drugs, devices and other therapies for patients. The program also is meant to increase contact between researchers and communities nationwide.

Awards, which vary in amount, have been given to 60 organizations - including the 14 that were announced Thursday.

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

"Just give them grants"

Source: *Science*. 2008 May 16;320(5878):849. Editorial.

Author(s): Alan I Leshner

<http://www.sciencemag.org/cgi/content/full/320/5878/849?maxtoshow=&HITS=10&hits=10&RESULTFORM AT=&fulltext=just+give+them+grants&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT>

The interdependent gold standards of a successful career in academic research are publication in prestigious journals and securing funding for one's independent research. There has been much discussion among scientists and funders about how best to launch such a career and how to fill the pipeline of young scientists to sustain the momentum of science (see also discussions at www.sciencecareers.org).

A major problem is that in many countries, research funding is quite constrained, so it's getting increasingly difficult for new investigators to secure their first grants. As a result, investigators are older and older when they finally begin independent work. On average, a recipient of a Starting Independent Researcher Grant from the European Research Council (ERC) is 35.6 years old and about 6 years past earning the Ph.D. New investigators supported by the U.S. National Science Foundation are also typically 6 to 7 years post-Ph.D. In the biomedical sciences, the average age at which an investigator first obtains a regular research grant from the U.S. National Institutes of Health (NIH) is 42 for a Ph.D. and 44 for MDs. No wonder there is concern about filling the pipeline of scientists. One has to wait until near middle age before getting one's own research program in full gear. (Next month, the American Academy of Arts and Sciences will release a report on supporting young investigators and high-risk-high-reward research.)

This prolonged wait for a grant is not the only problem. A new investigator often has to have completed two or three postdoctoral training periods before securing a tenure-track position. As emphasized in the U.S. National Research Council's 2005 report, *Bridges to Independence*, this extensive post-Ph.D. training, in which one often focuses on a mentor's research agenda rather than one's own, may stifle innovation and overly narrow young scientists' interests. If this is true, our models for postdoctoral training need revision.

Virtually every research funding agency has experimented with approaches to recruiting and funding young scientists, and many have been abandoned. Some small seed-grant programs were discarded because they didn't provide enough resources. Some special programs have included mentoring components on the basis of the argument that even after substantial postdoctoral training, young investigators would benefit from even more lab leadership training. And some special programs have been abandoned because their awards were more stigmatizing than beneficial. One such example is the FIRST Award (R-29) from the NIH, given up in part because many universities treated it as funding for those who could not get a "real" regular research grant, and thus it was not credited toward getting tenure. This argues for uniformity in how we support new investigators, instead of mounting special programs. One possibility

is to review new investigators as a group, rather than having them compete with more seasoned investigators with established track records and extensive preliminary data.

What should we do? If the consensus is that young scientists really need a regular research grant to launch their careers, why not simply tilt funding decisions more toward new investigators? After all, there are many more meritorious proposals from junior investigators--which have passed muster through peer review--than can be funded. The tilt would, of course, result in fewer senior investigators getting funded or receiving multiple grants, but if we are genuinely concerned about the pipeline, we will need to make this tradeoff.

Some such initiatives have begun. Last year, the proportion of NIH research grants going to new investigators was over 25% for the first time in nearly a decade. The ERC plans to award about one-third of its frontier research funding as Starting Grants. And the United Kingdom's Medical Research Council is providing protected research time for younger faculty through New Investigator Research Grants.

These endeavors are clearly a start, but the number of young investigators being funded is still relatively small. More such efforts are needed to encourage young scientists who are contemplating research careers and to foster innovation and creativity while they are at their peak. This would demonstrate a real commitment of the scientific enterprise to ensuring its own continuity.

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10. PHARMACEUTICAL INDUSTRY

"Gilead, Boehringer freeze prices on AIDS drugs to U.S. agencies"

Date: 03 June 2008

Source: *Bloomberg News*

Author(s): John Lauerman

<http://www.bloomberg.com/apps/news?pid=newsarchive&sid=aRd1TFxtLp84>

Gilead Sciences Inc. and Boehringer Ingelheim GmbH will freeze prices on their AIDS drugs for certain government agencies in the U.S., a patient treatment and advocacy group said today.

Gilead, maker of the AIDS pill Truvada, will suspend price increases to three U.S. and state government agencies through Dec. 31, 2010, according to the AIDS Healthcare Foundation, which provides treatment for 77,000 patients in 22 countries. Boehringer, the world's largest family owned drugmaker, will freeze the price of its drug Aptivus for state AIDS programs through May 1, 2009, the Los Angeles-based foundation said in an e-mail today.

The foundation asked companies to halt price increases because of difficulties government programs have had in expanding access to life-saving AIDS drugs, the organization said. Abbott Laboratories, Bristol-Myers Squibb, GlaxoSmithKline Plc, Merck and Co., Pfizer Inc., Roche Holding AG, and Johnson and Johnson's Tibotec Therapeutics unit didn't agree to the request, the foundation said in the e-mail.

"We urge the other drug companies to follow BI's and Gilead's lead and to freeze price increases that create an unnecessary burden on an already overburdened public health system and keep lifesaving drugs out reach for those who need them," said Michael Weinstein, president of the foundation, in the statement.

About 3 million patients in low- and middle-income countries are getting effective AIDS treatment today, about one-third more than in 2006, the Geneva-based World Health Organization said yesterday. About 33 million people worldwide are infected with the human immunodeficiency virus, or HIV, that causes AIDS, according to the WHO.

Three Agencies

Gilead of Foster City, California, will freeze prices on all its AIDS drugs -- Viread, Truvada and Emtriva -- for the U.S. Public Health Service, the Federal Supply Service, and the state AIDS Drug Assistance Programs, said Amy Flood, a company spokeswoman. Worldwide sales of Gilead's AIDS drugs last year totaled \$3.14 billion, she said.

The wholesale acquisition cost, the price paid by drug wholesalers, of Gilead's Viread is \$552 a month, \$329 a month for Emtriva, and \$840 a month for Truvada, Flood said. Government purchasers generally get partial rebates from these prices, she said.

"We share your concern regarding antiretroviral cost pressures face by government payers, particularly during times of limited budget access and flat funding," said Gregg Alton senior vice president and general counsel for Gilead, in a letter to the foundation.

Boehringer spokeswoman Judith von Gordon didn't return calls seeking comment after the close of business hours.

Boehringer of Ingelheim, Germany, has already reduced the price of its drug Viramune to 60 cents a day in 78 low-income countries, and \$1.20 a day in 67 middle-income countries, officials said in a letter to the foundation. The price freeze on Aptivus will apply to sales to state AIDS Drug Assistance Programs, and became effective May 1, the letter said.

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11. ANNOUNCEMENTS

Taking HIV Prevention to the Next Level: A Field Perspective

www.jhpiego.org

A frontline account from Jhpiego's global health professionals on successes and challenges in the worldwide battle against HIV/AIDS. Jhpiego's experts will discuss key areas of HIV/AIDS prevention, including family planning and HIV integration, prevention of mother-to-child transmission, and other evidence-based strategies.

Hosted by The Hon. Barbara Lee. Speakers include:

- Dr. Leslie Mancuso, Ph.D., RN, FAAN, Jhpiego President and CEO
- Dr. Pamela Lynam, Jhpiego Country Director, Kenya
- Dr. Emmanuel Otolorin, Jhpiego Country Director, Nigeria
- Dr. Lucito Jeannis, Jhpiego Country Representative, Haiti

About Jhpiego

Jhpiego's (ja-PIE-go) mission is to enhance the health and save the lives of women, children and families in limited-resource settings throughout the world. For nearly four decades, Jhpiego has put evidence-based health innovations into everyday practice to overcome barriers to high-quality health care services for the world's most vulnerable populations. From its origins as technical experts in reproductive, maternal and child health, Jhpiego has grown to embrace new challenges, including prevention and treatment of HIV/AIDS, malaria and cervical cancer.

Towards Universal Access: Scaling up priority HIV/AIDS interventions in the health sector

<http://www.who.int/hiv/mediacentre/2008progressreport/en/index.html>

The end of 2007 marks an important step in the history of the HIV epidemic. According to the WHO, UNAIDS and UNICEF report *Towards Universal Access: Scaling up Priority HIV/AIDS Interventions in the Health Sector*, nearly a million more people (950,000) were receiving treatment with antiretroviral therapy (ART) in low- and middle-income countries by year's end, bringing the total number of recipients to close to 3 million - a more than seven-fold increase over four years.

The WHO/UNAIDS '3 by 5' initiative, which sought to have 3 million individuals on treatment by 2005, is widely credited with jump-starting the global effort to provide widespread ART access to people in need living in low- and middle-income countries.

In 2007, that target was achieved a scant two years after the 2005 deadline. Not only has the number of people receiving treatment increased dramatically, but the pace of scale-up has also accelerated.

The year 2007 also saw gains in access to interventions designed to prevent mother-to-child transmission (PMTCT), as well as increased testing and counselling and greater country commitment to male circumcision. An increasing number of children are also benefiting from paediatric ART programmes. At the end of 2007, an estimated 200,000 children were receiving ART compared to 127,000 in 2006 and 75,000 in 2005.

Nevertheless, countries are still far from meeting universal access goals. An estimated 2.5 million people were newly infected with HIV in 2007, and overall, ART coverage still remains low - only 31% of people estimated to be in need of treatment in low- and middle-income countries were receiving it in 2007.

Moreover, weak health systems and, in particular, a critical shortage of health-care personnel and a lack of long-term sustained funding threaten efforts to achieve universal access to HIV prevention, treatment and care. At the end of 2007, the gap between required and available funding was estimated to be US\$ 8.1 billion. To meet universal access

targets, funding will have to more than quadruple to US\$ 35 billion in 2010 and to US\$ 41 billion in 2015.

EDITOR'S NOTE: The full report is available for public download at the above website. A media write-up of the report is available for public access at

<http://www.nytimes.com/2008/06/03/world/africa/03aids.html?partner=rssnyt&emc=rss>

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