



# ALLIANCE FOR MICROBICIDE DEVELOPMENT

**09 November 2007, Volume 8, Number 44**

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

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

Its purpose is to:

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

The *News Digest* is produced in a web-based format. Readers can view complete issues of the Digest or search by keyword for individual articles at <http://www.microbicide.org/publications/>. If you would like to be removed from the *Digest* distribution list, please send an email to [digest@microbicide.org](mailto: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. MEDIA COVERAGE OF MICROBICIDES

#### "Conference offers look at future AIDS prevention product"

**Date:** 08 November 2007

**Source:** *The Daily Northwestern*

**Author(s):** Tiffany Wong

[http://www.dailynorthwestern.com/home/index.cfm?event=displayArticle&uStory\\_id=88b1849a-f44f-4ea0-816d-74167c6ad918](http://www.dailynorthwestern.com/home/index.cfm?event=displayArticle&uStory_id=88b1849a-f44f-4ea0-816d-74167c6ad918)

The solution to AIDS sounds a lot smaller than the epidemic it is meant to overcome: **microbicides**. The Center for Global Engagement, GlobeMed and World Resources Chicago sponsored a conference on **microbicides** and HIV/AIDS on Wednesday.

The conference featured leading activists in the field, including Michael Diamond, president of World Resources Chicago; Jim Pickett, director of advocacy at the AIDS Foundation of Chicago and Dr. Harry Moultrie, pediatrician at Harriet Shezi Pediatric AIDS Clinic in Soweto, South Africa.

**Microbicides** are a new class of products under development that a woman could use vaginally to protect herself and her partner from HIV and other sexually transmitted infections, according to the conference's Web site. They have the potential to be produced as a gel, cream, sponge or intra-vaginal ring that could be used for months at a time.

There is also a movement to develop rectally inserted **microbicides** for men who have sex with men as well as for women, since the number of women engaging in anal sex is on the rise, Pickett said. Many leading scientists believe that **microbicides** are the future of HIV prevention and that it is likely that they will be available before an effective vaccine is found.

According to a mathematical model developed by researcher Richard Hayes, if 20 percent of people in 73 countries use a 60 percent effective **microbicide** during half of their sexual activities, 2.5 million cases of HIV infection will be avoided. The focus would be on countries in Sub-Saharan Africa, where more than 25 million people are infected.

As a pediatrician in South Africa, Moultrie witnessed many aspects of the "incredible crassness, violence and discrimination" that AIDS patients face in Africa.

"Take your child home, let your child die, don't waste my time," was the typical response of many doctors to mothers with HIV-infected children, Moultrie said. Complicating the matter is the fact that South African President Thabo Mbeki does not believe HIV causes AIDS, he said.

While the prospect of eradicating the HIV/AIDS epidemic seems more palpable with the development of **microbicides**, there is a long way to go before there will be an effective **microbicide** on the market, according to conference speakers.

"In terms of **microbicides**, we are at the boombox stage," said Pickett, drawing on the analogy of music players evolving from the "ugly, clumsy phase" to the smaller modern iPods and MP3 players.

The current problem **microbicide** researchers are facing is a lack of funding, Moultrie said. The current budget for **microbicide** research under the President's Emergency Plan for AIDS's Relief is \$144 million. Conducting a study may cost anywhere from \$60 to \$80 million.

The **Microbicide** Development Act, which would provide for more funding, is currently under debate in Congress. Sen. Barack Obama (D-Ill.) is one of the main supporters of the bill, but there are still many "recalcitrant Illinoisans" who will not sign on to the bill, Pickett said.

Pickett encouraged the audience to call their senators and representatives to support the bill.

"It can be a simple message," Pickett said, displaying a method of effectively contacting congressmen.

"**Microbicides** are the future," said Harishi Patel, a University of Illinois-Chicago alumnus who works with HIV patients in Uganda and came to the lecture to network and learn more about the stories of the people hosting the conference.

"Hearing these people's stories fuels me to continue with my work," Patel said.

### "Anti-HIV vaginal gel gets green signal for phase III trial"

**Date:** 06 November 2007

**Source:** *The Indian Express*

**Author(s):** Anuradha Mascarenhas

<http://www.indianexpress.com/story/236340.html>

As many as 100 HIV uninfected women from Pune have successfully completed the phase II trial of the Tenofovir **vaginal gel** - a **microbicide** - that women can use to protect themselves against HIV. Another 100 women in the US have also nearly completed the trial.

"With the completion of the crucial phase II trial, this gel will now move on to the third phase to test its efficacy in preventing HIV transmission," Dr Smita Joshi, project in-charge and senior research officer at the National AIDS Research Institute (NARI), told The Indian Express on Monday.

The trial was conducted by NARI at the Jehangir hospital in Pune. A part of the HIV Prevention Trial Network (HPTN) project, it was funded by the National Institutes of Health, USA. "Basically, vaginal **microbicides** will help women protect themselves against HIV and other sexually transmitted infections when they cannot negotiate condom use by men," Joshi said.

The phase I of the trial was conducted in the US in 2004 to assess the safety of Tenofovir gel manufactured by US-based Gilead Pharmaceuticals. "Phase II assessed the long-term safety of the drug and the 100 participants were enrolled both in Pune and the US for six months. We wanted to assess the long-term safety of the product," Joshi said.

When contacted, Dr Namita Chandhiok, deputy director, Indian Council of Medical Research (ICMR), said they had been looking for a product that can empower women. "While last year was bad in terms of **microbicides** for HIV prevention, the government is now hoping that the second generation anti-retroviral drugs which are more specific can yield results."

"ICMR is planning more clinical trial sites to test more **microbicides** products," said Dr Badri Saxena, professor at the Centre for Policy and Research who hosted the workshop on regulatory pathways for **microbicides** in Asia, last week. "The current use of HIV controlled methods such as abstinence, monogamy and condoms are not always feasible."

"**Microbicides** have been billed as a female-controlled HIV prevention method. Even though most women like the idea that they could use such a product without informing their partners, most would nevertheless prefer to tell their regular partners if they are using a **microbicide**," according to studies presented at the **Microbicide** 2006 conference. "Some want to disclose the use of **microbicides** to enhance intimacy while others believe that gel-based lubricants would be detectable to their partners, triggering negative consequences."

Research indicates that a woman seeks her husband's approval before using a vaginal product and that male partners will not permit their wives to use a **microbicide** with an STI/HIV indication. "Hence there is an urgent need to have other HIV prevention technologies which are women initiated methods," said Chandhiok.

### "Extended Interview: U.S. Global AIDS Coordinator Mark Dybul"

**Date:** 06 November 2007

**Source:** *Global Health Council*

[http://www.pbs.org/newshour/bb/health/july-dec07/dybul-extended\\_11-06.html](http://www.pbs.org/newshour/bb/health/july-dec07/dybul-extended_11-06.html)

**EDITOR'S NOTE:** *The following is an excerpt from the transcript of the Global Health Council's interview with Ambassador Mark Dybul, U.S. Global AIDS coordinator of the president's AIDS initiative known as PEPFAR, as he talks about the program's impacts, challenges and future. Please visit the above website for the entire interview.*

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#### *Abstinence requirement*

SUSAN DENTZER: A big discussion is being had and will continue to be had on earmarks and set-asides, and in particular the prevention component of that. The Institute of Medicine report on PEPFAR said that many people feel that particularly the abstinence requirement and the set-asides have been an issue. We also heard from people in the field that as abstinence monies get shoveled out the door, and implementing partners have to use those abstinence monies, they feel sometimes they're put in a position where they're in violation of the guidelines, depending on what they are able to use those abstinence monies for. This echoes the problem that the report commented on. Going forward, how should this be dealt with?

MARK DYBUL: Well, I think it's important to note the IOM criticized all directives. Remember, the IOM is a scientific group, and from a high level kind of detached scientific perspective, they're quite right. What do you need directives for? Just go to work in the countries and figure things out.

That is probably true, but from a policy standpoint, from the standpoint of trying to have the most effective program to optimize the use of resources, we have to look a little bit differently. The administration actually supports only two directives going forward, not the whole list of directives that existed the last time. But those directives were important.

The reason directives are important is because they direct. They redirect in many ways from where we were. So, for example, three years ago the US government was spending almost nothing on treatment. We needed a directive at that point to insure that we committed the resources for treatment. Now we've done that, we don't need it any longer.

Orphans and vulnerable children we had not committed much to before. When the emergency plan started, only \$30 million across the entire US government went for orphans. Now it's around \$270 million dollars for orphans. But it's still difficult to get commitment to orphans when we do our operations plans, and I think it's because there's not enough expertise, or the countries aren't as focused on it.

So we think we still need that 10 percent directive because when we make money available for orphan care, we don't see it utilized. So we need to continue to push on that.

How much longer I don't know. At some point it will become like treatment, and we don't need it. Same on prevention.

I think it's important to note that what our guidance is and what the law supports is comprehensive prevention. And again, it gets to direction and redirection. Before the emergency plan started, we were heavily one-prevention, one size fits all for prevention, which was a mistake. We took data from concentrated epidemics where small parts of the population are infected in Asia, Latin America, where we had effective programs - for example, in people in prostitution or intravenous drug users, and we took those data from concentrated epidemics and applied it to a generalized epidemic. And the data are overwhelming that that failed - nor surprisingly failed.

So what we needed to do was redirect our comprehensive program, which includes abstinence or delaying when you become sexually active, or secondary abstinence. There are data from Kenya and people who had been sexually active who are no longer sexually active. You need to be faithful to a single partner. We know that's very important in the epidemic. The data are overwhelming. That one piece, reduce your partners, has had a significant impact on generalized epidemics, and correct and consistent condom use.

We're also pushing forward on, for example, male circumcision which we believe will reduce prevalence, or HIV incidents further. We're hoping that pre-exposure prophylaxis or **microbicide** becomes available.

So we have this very comprehensive approach. We also then have prevention of mother to child transmission, safe blood, safe medical injections. So we have a very comprehensive approach.

What the directive does is insure we have that comprehensive approach so that we don't go back to applying principles from concentrated epidemics to generalized epidemics.

So we support some directive here to insure we have evidence based comprehensive prevention. Sen. Richard Lugar has introduced a bill. We actually support the language that is in that bill because it changes the previous directive in a way that we'll build on, and learn from what we've seen over the last couple of years in terms of effective prevention.

What the language says is how you apply that - these behavior change approaches apply to sexual transmission of HIV, which is 90 percent of the transmission in sub-Saharan Africa. It ought not to apply to prevention of mother to child transmission, or safe blood, or safe medical injection, or when we have them, **microbicides** or pre-exposure prophylaxis. But it's a behavior change, and that's - that makes a lot of sense, and therefore we - but we need that comprehensive approach.

It also talks about the difference between concentrated and generalized epidemic, following the epidemiology so you have the most effective approach in those countries.

We have very different approaches in a generalized epidemic in, for example, Kenya and Cambodia, because they're different epidemics, so you need a different approach. And that's what we've been doing. It simply is more codified in the law.

SUSAN DENTZER: Is that in effect saying that although the original law set forth this particular clear set-aside within the prevention bucket of abstinence, things have evolved, and now underneath the abstinence umbrella there's a much broader set of understandings of behavior change, including, as you said, partner reduction? It may not be abstinence purely speaking. It may be partner reduction, but that there is a much broader understanding of what these prevention initiatives ought to entail.

MARK DYBUL: Well, I think we've just learned how to implement them, but the original law allowed for all of that. It had abstinence and fidelity and correct and consistent condom use. It just had a directive related to insure that we had what's called abstinence, but it's really often delaying of sexual debut, or people who were sexually active not becoming sexually active, and this works very well. There have been studies to show that that's made a huge difference in epidemics.

So I think that the fundamental insight has changed. It's just in terms of how you apply it in a directive. And again, I think there will be a time when these directives aren't necessary. It's just not now. We're just not far enough along, and we can tell that from a policy perspective, which I think differentiates where we're going from the IOM.

The IOM is not looking at policy and implementation on the ground. They're looking at a purer standpoint, and again from a pure standpoint, why have a directive, you know. Just let the countries figure it out.

From a policy standpoint, that's not where we are yet. We're there on treatment, so we don't think we need that directive. We're there on care, except for orphans, so we don't need that directive, but we believe where we are right now means we still need directives for orphans, to protect the orphans and also to insure we have the most effective prevention strategy.

SUSAN DENTZER: Staying on prevention, many people have made the point that with 4 to 5 million new infections a year, it will be very difficult for the world to put everybody eventually on treatment, and that the - unless we want to consign ourselves to a future of constantly chasing our tail on this, there must be a dramatic cut in the rate of new infections. You mentioned some of the initiatives that one puts a lot of hope on - male circumcision, for example, the future development of a **microbicide**. What else can be done, as we think through the future of this program, to radically cut the rate of infection?

MARK DYBUL: Well, I think you've put your finger on what everyone is struggling with, and whether you're following your tail or turning off the tap, it's quite appropriate. We can't treat our way out of this epidemic.

That's one of the extraordinary things about the initiative. When the introduction of this initiative is remembered historically, it will not only be because it was the largest in history, it will be because it combined prevention, care, and treatment for the first time. No one had ever stood up and said, you can't just do treatment. You've got to include prevention with it. And you have to have care, too, as a comprehensive package. It's an extraordinary insight. The rest of the world isn't quite there yet.

So prevention has always been a bedrock of this epidemic and of this response of the American people. And if you look to "PEPFARTHER", as you called it, you'll see that the goals in prevention are actually growing higher than the goals in treatment and care, with that recognition that we need to do a better job of prevention.

What we're limited by is the science. As difficult as treatment is, it's actually easier than prevention because it's a medical intervention. Prevention is changing people's behavior right now, until we have a vaccine, or a **microbicide**, or pre-exposure prophylaxis, or some other technological interventions, we're relying on behavior change. And as we know from smoking campaigns and, you know, people - getting people to reduce fat content, and these types of health behavior change, it takes a long time.

I think actually we've made tremendous progress, given the short period of time that people have done these interventions. But what it means is really focusing on it, and what we're referring to it now as combination prevention. You can't just do one approach. You've got to do all approaches in a geographic area. And we're working with our international partners. We've got some exciting new initiatives, I think some of the most exciting things that will happen in HIV-AIDS, working on this concept of combination prevention.

So we think we need to concentrate on it more, use all the data available, which is what we've been doing. We're gathering more data, and fight the epidemic in terms of prevention. But I think people are getting a little bit too discouraged. I think we can do this. We've seen we can do it, whether it's Uganda, Kenya, Botswana, Namibia, South - parts of South Africa, Ethiopia, Nigeria. There's good reason to hope. We just have to concentrate on it and keep it up.

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## 2. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

### "Mucosal safety of PHI-443 and stampidine as a combination microbicide to prevent genital transmission of HIV-1"

**Author(s):** D\Cruz Osmond J, Uckun FM

**Reference:** N/A 88(4Suppl):1197-206.

<http://www.asco.org/portal/site/ASCO/menuitem.a3fb42726842a82627c4c291ee37a01d/?vgnextoid=d70b3608f9958010VgnVCM100000f2730ad1RCRD&index=n&pmid=17498709>

**Published Abstract:** OBJECTIVE: To investigate the in vitro and in vivo mucosal safety of a nonnucleoside reverse transcriptase (RT) inhibitor (PHI-443) and a nucleoside analogue RT inhibitor (stampidine)-based anti-HIV **microbicide** either alone or in combination. DESIGN: In vitro and in vivo studies using three-dimensional vaginal epithelia integrating Langerhans cells and 16 New Zealand White rabbits, respectively. SETTING: Research laboratory. INTERVENTION(S): Rabbits in groups of four were exposed intravaginally to a gel with and without 1% PHI-443, 1% stampidine, or 1% PHI-443 plus 1% stampidine for 14 days. Cytokine/chemokine release by three-dimensional co-cultures in the presence and absence of PHI-443 or stampidine. MAIN OUTCOME MEASURES(S):

Histologic scoring of vaginal tissue for mucosal toxicity at 24 hours after dosing. Simultaneous evaluation of levels of 10 cytokines (granulocyte-macrophage colony-stimulating factor, interleukin-1alpha, interleukin-13, macrophage inflammatory protein-1beta, granulocyte colony-stimulating factor, interleukin-18, tumor necrosis factor-alpha, interleukin-6, interleukin-1beta, and interferon-gamma) and 6 chemokines (epithelial neutrophil-activating peptide-78, interleukin-8, monocyte/macrophage chemoattractant protein-1, macrophage inflammatory protein-3alpha, interferon-inducible protein-10, and regulated upon activation of normal T-cell expressed and secreted) in culture media by a multiplexed chemiluminescence-based immunoassay. **RESULT(S):** In the rabbit model, repeated intravaginal administration of PHI-443 plus stampidine via a gel formulation at concentrations nearly 2,000 and 10,000 times higher than their respective in vitro anti-HIV IC(50) values did not result in vaginal irritation. The levels of proinflammatory cytokines/chemokines secreted by multilayered human genital epithelia integrating Langerhans cells were unaffected by prolonged exposure to PHI-443 or stampidine. **CONCLUSION(S):** The combination of PHI-443 and stampidine was noncytotoxic to vaginal epithelial cells, nonirritating to vaginal mucosa, and did not induce the secretion of proinflammatory cytokines and chemokines by co-cultures of human genital epithelia and Langerhans cells. These attributes are particularly useful for the clinical development of PHI-443 and stampidine as a combination **microbicide** and as a prophylactic anti-HIV agent to curb genital transmission of HIV-1 by semen.

### **"Phagocytic function of human blood polymorphonuclear leukocytes in the presence of carrageenan, a potential vaginal microbicide"**

**Author(s):** Malawista SE, de Boisfleury Chevance A

**Reference:** N/A 30(5):131-35.

<http://www.springerlink.com/content/2448807g6474j073/>

**Published Abstract:** Carrageenan is currently undergoing clinical trials as the active constituent of a **vaginal gel** product for use as a female-controlled option to prevent the transmission of HIV during sexual intercourse. Here we show that in the presence of 0.5 mg/ml of carrageenan, human blood polymorphonuclear leukocytes (PMN) do not ingest this material, as evidenced by a lack of progressive vacuolization, but can ingest microorganisms present in the medium, excluding adjacent carrageenan. Moreover, PMN move at normal speeds, respond chemotactically, and reduce nitroblue tetrazolium (NBT) to formazan on stimulation. Hence, in the presence of carrageenan the phagocytic response appears to remain intact.

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### **3. PUBLISHED RESEARCH: RELEVANT BASIC AND TRANSLATIONAL SCIENCE**

#### **"Direct stringency comparison of two macaque models (single-high vs. repeat-low) for mucosal HIV transmission using an identical anti-HIV chemoprophylaxis intervention"**

**Author(s):** Subbarao S, Ramos A, Kim C, et al

**Reference:** N/A 36(4-5):238-43.

<http://www.ingentaconnect.com/content/mksg/jmp/2007/00000036/F0020004/art00008;jsessionid=3p1i918f7qrg6.alice?format=print>

**Published Abstract:** *Background* In our previous work, oral chemoprophylaxis with tenofovir disoproxil fumarate (TDF) provided partial protection in rhesus macaques against repeated low-dose (RL) intrarectal SHIV162p3 exposure. *Methods* Here, we make a direct comparison of these previous findings with data generated using a single high (SH)-dose challenge strategy. *Results* All 5 (100%) control macaques were infected after a SH challenge and only three of five (60%) TDF-treated macaques became infected. The remaining two TDF-treated macaques remained virus-negative and were susceptible to virus infection upon re-challenge in the absence of oral TDF. Thus, two of five (40%) TDF-treated macaques were protected by the pre-exposure chemoprophylaxis regimen. By comparison with the RL challenge system, only one of four (25%) of TDF-treated macaques were protected from infection, whereas four of four (100%) control macaques became infected using RL challenges. *Conclusion* Taken together, these findings indicate that the stringency of the RL challenge model for testing antiretroviral interventions is not lower and possibly greater than that of the SH challenge model.

#### **"Effect of genital ulcer disease on HIV-1 coreceptor expression in the female genital tract"**

**Author(s):** Sheffield JS, Wendel GD, McIntire DD, et al

**Reference:** N/A 196:1509-16.

<http://www.journals.uchicago.edu/JID/journal/issues/v196n10/38060/brief/38060.abstract.html>

**Published Abstract:** *Objective.* To examine the expression of human immunodeficiency virus type 1 (HIV-1) coreceptors (CCR5 and CXCR4) by monocytic cells within human genital ulcers. *Methods.* Women with primary or secondary syphilis, herpes simplex virus type 1 (HSV-1) or HSV-2 infection, or noninfectious abrasions had a biopsy sample taken from the lesion and contralateral vulva. HIV-1 coreceptor expression on CD3+ and CD14+ cells was analyzed by flow cytometry. Real-time reverse-transcriptase polymerase chain reaction was used to assess levels of coreceptor mRNA expression. *Results.* Women with primary or secondary syphilis or with HSV-1 or HSV-2 infection had significantly increased numbers of CD14+ cells expressing CCR5 within the genital ulcer. This increase was also noted in the nonulcerated tissue isolated from women with syphilis and in peripheral blood mononuclear cells from women with secondary syphilis. CCR5 mRNA expression was increased in tissue obtained from syphilis lesions. *Conclusions.* Monocytes recruited to genital ulcer disease (GUD) sites express increased levels of CCR5. This increased expression could account, at least in part, for enhanced HIV-1 transmission in the setting of GUD.

#### **"Gradations of researchers' obligation to provide ancillary care for HIV/AIDS in developing countries"**

**Author(s):** Richardson HS

**Reference:** N/A 97(11):1956-61.

<http://www.ajph.org/cgi/content/abstract/97/11/1956>

**Published Abstract:** Three principal factors affect the stringency of medical researchers' obligation to provide antiretroviral treatment to participants in non-HIV/AIDS studies that are conducted in developing countries: (1) the centrality of HIV/AIDS to the study design, (2) the extent of the researcher - participant interaction, and (3) the cost relative to the study budget. I provide a basis for assessing the comparative stringency of the researchers' obligation to provide this type of ancillary care. Practically, given the range of possible responses to study participants' needs, calibrating the researcher's responsibility to provide ancillary care is a useful step in ethical analysis. Theoretically, a gradation of obligation suggests how research ethics committees or institutional review boards can take multiple, potentially conflicting ethical factors into account without undertaking spurious efforts to quantify their importance.

**"Herpes Simplex Virus (HSV) suppression with valacyclovir reduces rectal and blood plasma HIV-1 levels in HIV-1/HSV-2-seropositive men: A randomized, double-blind, placebo-controlled crossover trial"**

**Author(s):** Zuckerman RA, Lucchetti A, Whittington WL, et al

**Reference:** N/A 196:1500-08.

<http://www.journals.uchicago.edu/JID/journal/issues/v196n10/38641/brief/38641.abstract.html>

**Published Abstract:** *Background* Herpes simplex virus type 2 (HSV-2) infection is common among human immunodeficiency virus (HIV)-infected persons, and HSV reactivation increases plasma and genital HIV-1 levels. We studied HIV-1 levels during HSV suppression in coinfecting persons in a placebo-controlled crossover trial. *Methods.* Twenty antiretroviral therapy (ART)-naive HIV-1/HSV-2-seropositive men who have sex with men in Lima, Peru, with CD4 cell counts less than 200 cells/L were randomized to receive either valacyclovir at 500 mg twice daily or placebo for 8 weeks, after which they underwent a 2-week washout period and then received the alternative regimen for 8 weeks. Specimens included daily anogenital swabs (for HSV DNA polymerase chain reaction [PCR]), thrice weekly rectal mucosal secretions (for HIV-1 RNA and HSV DNA PCR) obtained by anoscopy, and weekly plasma (for HIV-1 RNA PCR). Outcomes were rectal and plasma HIV-1 RNA levels by treatment arm. *Results.* HIV-1 was detected in 73% of 844 rectal and 99% of 288 plasma specimens. HSV was detected in 29% and 4% of mucocutaneous specimens obtained during placebo and valacyclovir administration, respectively (P (less than) .001). Valacyclovir resulted in a 0.16 (95% confidence interval [CI], 0.07-0.25; P = .0008; 33% decrease) log<sub>10</sub> copies/mL lower mean within-subject rectal HIV-1 level and a 0.33 (95% CI, 0.23-0.42; P (less than) .0001; 53% decrease) log<sub>10</sub> copies/mL lower plasma HIV-1 level, compared with values for placebo. *Conclusions.* Valacyclovir significantly reduces rectal and plasma HIV-1 levels in HIV-1/HSV-2-coinfecting men. HSV suppression may provide clinical benefits to persons not receiving highly active ART as well as public health benefits.

**"Reducing publication bias of prospective clinical trials through trial registration"**

**Author(s):** Abaid LN, Grimes DA, Schulz KF

**Reference:** N/A 76(5):339-41.

**Published Abstract:** Publication bias is the selective publishing of favorable or statistically significant results. This practice, over time, distorts the medical literature by depicting inordinately optimistic outcomes for treatments and interventions. Sources of publication bias include preferential publishing by journals and preferential submission by researchers. Mandatory trial registration, as instituted by the International Committee of Medical Journal Editors (ICMJE), should reduce publication bias by improving the ability to identify all trials pertaining to a specific intervention. Contraception endorses the views of the ICMJE and will now require registration of all prospective trials.

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#### 4. EPIDEMIOLOGY

##### "New danger in Africa: HIV-TB combined epidemic"

**Date:** 02 November 2007

**Source:** *Indo-Asian News Service*

<http://in.news.yahoo.com/071102/43/6mqj0.html>

A deadly combination of HIV and tuberculosis (TB) is rapidly spreading in sub-Saharan Africa and has gone largely unnoticed so far.

Health systems, moreover, are not adequately equipped to diagnose, treat or contain the co-epidemic due to unanswered scientific and medical questions, according to a report issued Thursday by The Forum for Collaborative HIV Research here.

The report notes that approximately one-third of the world's 40 million people with HIV/AIDS are also infected with TB and the mortality rate due to the co-epidemic is five-fold higher than that for tuberculosis alone.

'The eye of the storm is in sub-Saharan Africa, where half of all new TB cases are HIV co-infected, and where drug-resistant TB is silently spreading,' said Veronica Miller, one of the authors of the report. 'Unlike bird flu, the global threat of HIV-TB is not hypothetical. It is here now. But the science and coordination needed to stop it are utterly insufficient,' she said.

The HIV-TB co-infection was first detected 23 years ago. Without proper treatment, 90 percent of people living with HIV die within months of contracting TB.

**EDITOR'S NOTE:** *The report, entitled "HIV-TB Co-Infection, Meeting the Challenge," is available at <http://www.hivforum.org/uploads/TB/Final%20HIV-TB%20Report.pdf>.*

## 5. OTHER PREVENTION APPROACHES

### "Coffee condoms promote safe sex in Ethiopia"

**Date:** 03 November 2007

**Source:** *The Guardian*

**Author(s):** David Batty

<http://www.cdcnpin.org/scripts/display/NewsDisplay.asp?NewsNbr=49480>

About 300,000 coffee-flavored condoms were sold in one week in Ethiopia, according to the US charity DKT International, which launched the condom promotion in September to fight HIV/AIDS. Coffee is thought to have originated in Ethiopia, and the public's enthusiasm for the drink has helped the campaign. An estimated 2.1 percent of Ethiopians have HIV, and in the capital, Addis Ababa, the proportion is more than 7 percent, said DKT International. In the capital's cafes, the flavored condoms sell for about 1 birr (US 11 cents), or about half the cost of a cup of coffee, a much cheaper price than other brands. The condoms are dark brown and have the aroma of a macchiato, a popular drink in Ethiopia consisting of espresso with healthy amounts of cream and sugar. 'Everybody likes the flavor of coffee,' a DKT International spokesperson said. The condoms were developed in response to complaints by some users about the scent of plain latex condoms. The charity has tailored flavored condoms to fit local preferences elsewhere, including a durian-flavored condom for Indonesia, and a sweetcorn-scented condom for China.

### "Male sex workers play Russian roulette with HIV"

**Date:** 02 November 2007

**Source:** *PlusNews*

<http://www.plusnews.org/report.aspx?ReportId=75115>

Shujaat\* plies his trade well. As dusk falls on the Pir Wadhai bus station in the Pakistani city of Rawalpindi, the slender 19-year-old gauges disembarking passengers for that 'look' - a responsive glance or wink suggesting a desire for more than just a quick bus ride home.

"Here you can find all sorts; mostly truckers, soldiers, day labourers, and of course married men," he said, leaning against the wall. "I always find someone," the now veteran male sex worker (MSW) boasted.

After three years on the streets, Shujaat's confidence is dwarfed only by his ambivalence towards contracting HIV - a virus that he and other men who have sex with men (MSM) are increasingly at risk of.

"I'm careful and I'm clean, so what's the problem?" he asked.

But for medical experts in Pakistan, a nation which until recently enjoyed a low prevalence for the virus, this line of thinking is worrying. The South Asian nation of more than 160 million inhabitants now faces a concentrated epidemic

among certain high risk groups - particularly intravenous drug users (IDUs), estimated at close to 200,000. In the country's commercial capital of Karachi alone, a reported 30 percent of IDUs are infected with HIV. Pakistan's National AIDS Control Programme (NACP) officially confirms just over 3,000 HIV/AIDS cases across the country, while health experts assess the real numbers to be much higher. According to UNAIDS, about 85,000 people are living with HIV in Pakistan today.

And while the issue of IDUs is often discussed in the media, the issue of MSM is usually ignored; a troubling reality in conservative Pakistan, where homosexuality is not only not discussed - it is often denied.

#### *The male sex worker - a taboo subject*

"It is very difficult to talk about sex and sexuality in Pakistan and more difficult to talk about homosexuality," said Dr Naeem-ud-Din Mian, chief executive officer for Contech International Health Consultants, a local NGO recently assigned a five-year project for the delivery of preventive services for MSM in the city of Faisalabad by the Punjab AIDS Control Programme and the World Bank.

Echoing that, Brian Miller, field coordinator for the Organisation for Social Development, a local NGO running an outreach programme near Pir Wadhai remarked: "People know about it, but it's a taboo subject as it's not in keeping with Pakistan's Islamic social setting."

As a result, open discussion about MSWs is all but impossible, despite the fact that most health experts in the country now view MSM, many of whom are married, as the singular most at-risk group after IDUs - and an important bridging population into mainstream heterosexual Pakistani society.

Government health figures reveal prevalence rates among IDUs of up to 27 percent, with around seven percent among MSM. According to the Infection Control Society of Pakistan (ICSP), another NGO targeting the prevention of HIV/AIDS among MSWs in Karachi, around half of the MSWs in the city are married, while more than half of the unmarried MSWs buy sex from female sex workers - underscoring the group's capacity to act as a conduit to the virus's spread.

"They're the next risk group," Naseer Muhammad Nizamani, country director for Family Health International (FHI) in Islamabad - which is actively engaged in promoting safer sex practices among MSM and MSWs in the country - said about MSWs. The US-based NGO estimates that there are some 50,000 MSWs in Pakistan, while others estimate their numbers are much higher.

ICSP says that in Karachi alone, there are between 40,000 and 50,000 MSWs, depending on the criteria used.

#### *The impact of poverty*

Although many MSWs are gay, poverty, lack of job opportunities and broken homes appear to be the driving force behind this activity. The majority of MSWs are below the age of 24 and began work at the age of 16, with many starting out under the guise of providing massage to men.

Today 'Malishias' - as they are commonly known - have become a common euphemism for sex in Pakistan, attracting their clients by massaging their private parts and masturbating.

"Massage boys are a traditional way of this happening. It's a big business in Pakistan," Nizamani said.

The average charge per sex act averages between just US\$1 and \$3. Pricing in turn largely dictates the number of clients a boy may be prepared to service on a given day. According to an NACP survey carried out in eight separate cities, most MSWs average 2.3 customers a day or more than 31 a month. This is even higher among members of the 'Hijra' (transgender) community.

One Hijra, who had no other source of income, said she could easily service up to 20 men in a single day.

"There is no limit to the number of customers and no limit to the service," she told IRIN/PlusNews openly.

#### *Insufficient services and low condom use*

Despite such candour, however, there are limits to levels of awareness among MSWs, most of whom have no real understanding as to how the virus is contracted or simply fail to use condoms to protect themselves.

"People have heard of AIDS. But when you go deeper into what proportion actually know how the disease is contracted, that's something else," FHI's Nizamani said.

Although the NACP survey revealed that 70 percent of MSWs knew something about HIV and that a large majority of those who had heard about HIV also knew that it could be transmitted through sexual intercourse, less than half knew that injections could transmit HIV.

In Karachi, ICSP found that just 18 percent of MSWs in that city knew about HIV, its preventions and modes of transmission, while the NACP survey found that only about 60 percent reported condom use as an HIV prevention method - a fact largely dictated by money.

"I don't use a condom," 25-year-old Javed, who works in Rawalpindi, told IRIN/PlusNews. "They [the customers] complain that they don't feel the same amount of pleasure."

"If the customer wants to have sex without a condom and is willing to pay for it, how can I refuse?" another MSW, who declined to give his name, said.

Less than 25 percent of MSWs reportedly used a condom for anal sex with their last client, and even fewer used any form of lubrication aside from saliva. According to Dr Kartar Lal of ICSP, 74 percent of MSM use saliva and oil in place of water-based lubricants, which facilitates the virus's spread.

"In-depth interviews of target groups revealed a significant proportion of these individuals are aware of the risks associated with unprotected sex, but are unable to negotiate safe sex practices with their partners," said Dr Rafiq Khanani, ICSP's president. The MSWs cite reasons of low self esteem, lack of empowerment and a genuine fear of losing the client to other sex workers willing to provide the service without a condom.

"It's very hard to speak openly about condom usage," Miller reiterated. "It's simply not done in a country like Pakistan." He said the government had done little to publicly support the use of condoms or their distribution, given the strong religious opposition in the country.

According to UNAIDS, less than 10 percent of people most at risk of contracting HIV, such as MSM and drug users, receive preventative services.

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## 6. POLITICS AND POLICY

### "Declare HIV/AIDS a 'humanitarian emergency'"

**Date:** 05 November 2007

**Source:** *IRINNews.org*

<http://www.alertnet.org/thenews/newsdesk/IRIN/06d4fdcc2cb117412d79960bbde834dd.htm>

The impact of HIV/AIDS in southern Africa, which has nine of the world's most affected countries, needs to be reassessed as a "humanitarian emergency" on its own, enabling interventions to be made timeously, a leading AIDS researcher argues in a new paper.

For this to happen, Alan Whiteside, director of the Health Economics and HIV/AIDS Research Division of the University of KwaZulu-Natal, South Africa, said in the paper, co-authored by researcher Amy Whalley, the conventional understanding of a humanitarian emergency has to be rethought.

"Traditional humanitarian thinking focuses on the short term, and is often aimed at returning affected populations to 'normality'," he said in Reviewing 'Emergencies' for Swaziland: Shifting the Paradigm in a New Era.

To make the point, the authors used Swaziland, which has an HIV prevalence rate of 33.4 percent among people aged between 15 to 49 years - the world's highest, according to UNAIDS - and the world's lowest life expectancy, just 31.3 years in 2004, as noted in the UNDP's Human Development Report. The paper was commissioned by Swaziland's National Emergency Council on HIV/AIDS (NERCHA).

The region also has eight other countries with some of the world's highest prevalence rates: Botswana 24.1 percent; Lesotho 23.2 percent; Namibia 19.6 percent; South Africa 18.8 percent; Zambia 17 percent; Mozambique 16.1 percent; Zimbabwe 15.6 percent, and Malawi 14.1 percent, according to UNAIDS.

"HIV/AIDS in Swaziland has been characterised by a slow onset of impacts that have failed to command an emergency response. With insufficient resource allocation and a lack of capacity, slow onset events can become emergencies," Whiteside maintained. The situation was not very different in the region's other affected countries.

Part of the problem was that, spurred by its consistent economic growth in the 1990s, Swaziland had been classified as a "low-middle-income country" by the World Bank, and a "medium human development country" by the UN Development Programme (UNDP). This classification altered the perception of the country in donor and international eyes as a 'poor' country to that of one able to support itself, restricting potential external funding.

Whiteside has tried to establish a correlation between the ever-increasing HIV prevalence recorded by national sero-sentinel surveillance surveys - which has shot up from 3.9 percent in 1992 to 42.6 percent in 2004 and declined

slightly to 39.2 percent in 2006 - and the falling social and economic indicators. "If negative trends were noticed earlier in Swaziland, some wider shocks may have been preventable".

Over the past 15 years, Swaziland has become characterised by a decline in economic growth, spreading poverty, and a rise in mortality and morbidity rates. "Current death rates now exceed the daily mortality thresholds used by agencies as an indicator of a disaster."

The number of people living below poverty line climbed from 65 percent in 1995 to 69 percent in 2001, while annual Gross Domestic Product (GDP) plunged from 6 percent in the 1990s to a current level of around 2 percent, resulting in negative per capita growth.

Whiteside said maize production had more than halved in AIDS-affected households and cited a 2004 study, A Systematic Review of the Economic Impact of HIV/AIDS on Swaziland, by F.T. Muwanga, published by the University of the Witwatersrand in Johannesburg, South Africa, showing that the average loss in GDP growth attributable to HIV/AIDS was around 1.6 percent per year.

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

### **"FDA failure on foreign inspections frightening"**

**Date:** 05 November 2007

**Source:** *in-Pharma Technologist.com*

**Author(s):** Kirsty Barnes

<http://www.in-pharmatechnologist.com/news/ng.asp?n=81098&m=1IPEN06&c=ctekxoihhlwjezb>

A US government audit has confirmed the Food and Drug Administration's (FDA's) continual lack of inspection of foreign drug manufacturing plants.

The revelation is frightening considering that 75-80 per cent of all active pharmaceutical ingredients (APIs) used by US drug manufacturers are now imported, mainly from India and China, along with 40 per cent of finished dosage forms from various global locations.

The worrying situation has long been highlighted by the US and EU industry trade bodies - the Synthetic Organic Chemical Manufacturers Association (SOCMA) and the European Fine Chemicals Group (EFCG) - who have been campaigning for regulators to increase their inspections of foreign facilities.

"The Asianisation of APIs has caught regulators by surprise and now they are having to play catch up," say the organisations.

The new Government Accountability Office (GAO) audit added more fuel to the fire, revealing that the FDA was unable to provide inspection records for two-thirds of the 3,250 facilities that are currently believed to supply the US with pharmaceutical ingredients.

The GAO also presented a similar report to Congress nearly ten years ago and it would appear during this time nothing much has changed. There has been an accelerating rate of change within the industry over the last 20 years, with massive globalisation of manufacturing occurring driven by the pressure to drive drug manufacturing costs down, and the FDA is becoming more and more overburdened.

At present the FDA only carries out inspections of around 7 per cent of the total number of foreign drug manufacturers a year, and at this rate, the GAO estimated that if the agency was to attempt to inspect the complete list of foreign suppliers even once, it would take over 13 years to do so.

According to the GAO report, China, which has the largest number of drug manufacturers eligible for FDA inspection (714) is earmarked for only 13 regulatory visits by the FDA this year, meaning only less than 2 per cent of the country's drug exporters will have their facilities examined.

However, it is China of all places that should be subject to particular regulatory scrutiny - over the past few years a spate of safety scares over Chinese-made drug substances has been well documented, along with numerous convictions of corruption amongst some of the country's high-ranking regulatory officials.

The FDA's inadequate computer systems are said to be to blame for much of the problem. The GAO found that the agency's databases contain conflicting information on foreign manufacturers, particularly in regard to the number of facilities that are subject to inspection, with the number sometimes differing by thousands, depending on which database is accessed.

"How can we have any confidence FDA is truly managing the risk that may come from foreign-made drug products if the FDA doesn't know the exact number or location of foreign drug manufacturers," Republican Bart Stupak said during the hearing.

The agency is well aware of this problem - in its 2008 budget it specifically requested \$247m (€170m) to modernise and implement new IT systems.

Meanwhile, the fossilised computer systems are not the thing holding the agency back. The foreign inspections that are carried out are not up to scratch, the GAO said, particularly referring to the double standards that the agency has for domestic and non-domestic manufacturers.

US drug makers are required to undergo surprise inspections every two years, while foreign manufacturers are not subject to any regular form of scrutiny and are given advance warning before an inspection takes place. Furthermore, the agency has to rely on translators provided by the foreign manufacturers themselves during the process.

During the congressional committee hearing on Thursday, pharma industry representatives branded this double standard as unfair, however, they insisted that they took responsibility for ensuring the quality of imported ingredients into their own hands, rather than relying on the FDA.

The US drug companies participating in the hearing said that they perform periodic inspections of the foreign plants where they source materials from and also perform random tests on the shipped product from time to time.

Despite the revelations of the GAO audit, the head of the FDA Dr Andrew von Eschenbach insisted that the US drug supply is safe.

In his testimony, he said that facility inspections are just one part of the agency's monitoring of foreign-made drugs. FDA approvals of new drugs include requirements regarding how and where a drug is manufactured, he said.

## **"New strategy for translational research creates new arrangements for clinical trials"**

**Date:** 05 November 2007

**Source:** *News-Medical.net*

[http://www.news-medical.net/print\\_article.asp?id=32193](http://www.news-medical.net/print_article.asp?id=32193)

The Medical Research Council (MRC) and the National Institute for Health Research (NIHR) have announced a new joint arrangement for clinical trials. The initiative forms a key part of the developing MRC- NIHR joint strategy for translational research.

As part of the strategy, a new clinical research programme called the Efficacy and Mechanism Evaluation (EME) Programme will be launched on 1 April 2008. The EME will be funded by the MRC, and administered by the NIHR as the lead organisation. The programme aims to support excellent clinical science with an ultimate view to improving health or patient care. Its remit includes clinical trials and evaluative studies which add significantly to our understanding of biological or behavioural mechanisms and processes, explore new scientific or clinical principles, evaluate clinical efficacy of interventions where proof of concept in humans has already been achieved and the development or testing of new methodologies.

The new strategy will see the EME programme working with the already established NIHR Health Technology Assessment (HTA) programme, to ensure that promising technologies are carried from the efficacy and safety stage through to being assessed for clinical and cost-effectiveness to the NHS. The HTA programme will continue to produce research information about the effectiveness, costs, and broader impact of health technologies for those who use, manage and provide care in the NHS.

The EME Programme will mainly work in responsive mode, taking applications from the research community and assessing them at regular intervals, although it may also fund proactively in particular areas of importance. Details of how to apply for funding will be available from January 2008.

Sir Leszek Borysiewicz, Chief Executive of the MRC said the new arrangements would help maintain the UK's place in leading how research is funded and carried out:

"More than sixty years ago the MRC developed a design for clinical trials that is recognised today as the gold standard - the randomised controlled trial. The MRC is delighted to be working with NIHR to provide new opportunities for late phase clinical trials. The partnership will enable us to take promising research and turn it into effective therapies more quickly and more efficiently. We will continue to play a major role in defining direction and strategy in clinical trials."

"This is an exciting collaboration between the MRC and NIHR in managing clinical research in the UK, and in bridging the gaps in translation of research into clinical benefit identified in the Cooksey Review," says Professor Sally Davies, Director General of Research and Development at the Department of Health, on behalf of the NIHR. "It allows new and existing research programmes to work more closely together to ensure that the excellent biomedical research

conducted in the UK is translated into excellent clinical research and real benefits for patients. Recent developments in the infrastructure for clinical research in the UK will facilitate rapid recruitment to trials."

Details of other components of the MRC-NIHR joint strategy for health research covering discovery and exploratory development, methodology and human capital will be announced separately.

The MRC and NIHR joint arrangement has been developed with the Office for Strategic Coordination of Health Research.

### **"Turning the brain drain from threat to opportunity"**

**Date:** 02 November 2007

**Source:** *SciDev.Net*

**Author(s):** David Dickson

<http://www.scidev.net/editorials/index.cfm?fuseaction=readEditorials&itemid=231&language=1>

Europe's recent bid to attract more skilled workers underlines developing countries' need for greater - not less - investment in their intellectual capital.

Listen to any developing country leader talk about the difficulties of building a knowledge-based economy, and chances are high that the brain drain will top their complaints. What is the point in investing in training cadres of scientists and engineers, they argue, if they immediately leave for better-paid jobs in the developed world?

So it is not surprising that last week's European Union announcement of plans to introduce a 'blue card' scheme to attract more highly skilled immigrants, particularly from Africa, Asia and Latin America, has raised strong protests within these regions (see 'EU 'blue card' to attract Southern researchers).

Many commentators are arguing that the move will only deepen and encourage the brain drain, and is likely to directly undermine commitments made elsewhere, at the G8 summit in Gleneagles in July 2005, for example, to build up strong professional communities in fields such as science and technology. One commentator described the EU announcement as a "neo-colonial grab for the raw materials of the information economy".

#### *Brain drain or circulation?*

The reality is more complex. Unlike politicians, development economists rarely talk of a brain drain: their preferred terminology is 'brain circulation' - the concept that individuals who leave a country can still make a valuable contribution to its development, either from a distance or by eventually returning.

This is not to deny that a major problem exists. Poor facilities and job prospects mean that in too many developing countries a science graduate's strongest hope of building a research career is to seek a position in a North American or European university.

Anecdotal evidence supports the statistics on the brain drain. It is not unusual to hear an Indian university's computer engineering department, for example, reporting that a whole graduation class plans to take up jobs in the United

States when they finish their studies. Or an African research department complaining that it is impossible to fill scientific vacancies since there are no qualified candidates left in the country.

Science and technology are far from being the only professional fields affected. Perhaps the worst hit is the medical profession. Trained nurses and health workers in countries such as Malawi are leaving to work abroad almost as fast as their countries produce them.

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

## **Malaria Forum Keynote Address - Bill and Melinda Gates**

<http://www.usglobalengagement.org/Portals/16/ftp/B&MGMalariaspch.pdf>

### **Prepared remarks by Bill and Melinda Gates, co-chairs**

*Melinda Gates:* Thank you for that very warm greeting. Bill and I welcome you here to Seattle - and we thank you for dedicating your lives to fighting malaria. You were working on these issues when no one was watching. The fact that so many more people know and care about malaria today is a testament to your vision, your persistence - and to the faith the world has in your work.

In the history of humanity, it's likely that no disease has ever caused more suffering, more sickness, and more death than malaria. Malaria symptoms were described in Chinese medical texts written nearly 5,000 years ago. The disease caused the decline of city-state populations in Ancient Greece, and untold deaths during World War II. Even now, a century after Nobel prizes were awarded for discoveries relating to malaria and its transmission, malaria is epidemic in many parts of the world. Malaria deaths worldwide peaked in the 1930s at nearly three and a half million and then began to drop with global efforts to fight the disease, reaching a low of about half a million at the end of the 1960s.

But then anti-malaria efforts dropped off, and the disease has been on the rise ever since. Now there are five hundred million cases of malaria every year and more than one million people die from it, mostly children. That's the equivalent of losing every student in the New York City public school system each year. We wouldn't let it happen here. We shouldn't let it happen anywhere.

But over the course of the last century, malaria changed from a disease that afflicted a broad range of countries to a disease that affected only poor countries. It changed from a celebrated cause of our scientists and politicians to a source of suffering that the rich world was willing to accept and the poor world was helpless to prevent.

Today, though, the world is coming back to this cause in large and enthusiastic numbers. UNICEF's report, released just yesterday, describes record levels of spending, distributing bednets, and delivering medicine. Global procurement of artemisinin-based combination therapies grew from 4 million doses in 2004 to 100 million doses in 2006. We also have record funding for research, more coordinated control efforts, and greater scientific tools than we've ever had before.

Bill and I believe that these advances in science and medicine, your promising research, and the rising concern of people around the world represent an historic opportunity not just to treat malaria or to control it - but to chart a long-term course to eradicate it. We know that the word "eradication" is troubling to many people with deep knowledge of malaria. It's an...audacious goal - to reach a day when no human being has malaria, and no mosquito is carrying it.

This is a long-term goal; it will not come soon. But to aspire to anything less is just far too timid a goal for the age we're in. It's a waste of the world's talent and intelligence, and it's wrong and unfair to the people who are suffering from this disease. The goal of eradicating malaria has the power to create great expectations, grand efforts, and record funding. When you ask people to donate time and money to save lives, they can be very generous. When you ask them to give time and money to eradicate a disease, their generosity can multiply. Those are the benefits. They are also the risks. If high energy and high expectations don't lead to success - it saps money and morale. People give up. Governments, foundations, and corporations cut their funding, malaria surges back - and gains can be quickly wiped out.

In 1955, the WHO vowed to eliminate malaria from the earth. The U.S. Congress put record sums of money behind the eradication effort - beginning in 1958. President Eisenhower was behind it, as was George Marshall, and Senator John Kennedy. Armed with DDT, chloroquine, money, and enthusiasm, the world made dramatic advances against the disease.

In Sri Lanka, malaria cases dropped from 1 million in 1955 to 18 cases in 1963. Not 18,000 - eighteen. Other countries showed similar gains. Optimism was so high that the young graduate student Andrew Spielman, who would later become an expert at Harvard on mosquitoes and disease, was told by his mentor at Johns Hopkins that he had chosen the wrong field. His mentor said, "By the time you've finished your thesis, all the insect-borne disease problems will be solved."

But the world was not ready for a long fight. As President Eisenhower said in a special message to Congress in 1957: "I propose that the United States join with other nations and organizations which are already spending over \$50 million a year on anti-malaria activities. In five years, these activities are expected to eradicate this disease."

The fight turned out to be more difficult than expected. Mosquitoes developed resistance to DDT and the parasite developed resistance to chloroquine. Gains were made, but eradication seemed remote - and so enthusiasm faded, funding slowed - and then everything unraveled. Control efforts were cut back, and when the disease began spreading again, populations were especially vulnerable - because people in areas where malaria had been made scarce had lost their immunity. Meanwhile, research into malaria had stopped because the world had been so confident of eradicating it - and so there were no new medicines, insecticides or insights. Over the next ten to fifteen years, the number of malaria cases increased by a factor of six in India and by a factor of nine in China.

Based on this history, some might argue that it's better simply to try to control malaria than to try to eradicate it - since trying to eradicate and then failing could be worse than never trying to eradicate at all. Why should we embrace the goal of eradicating malaria instead of controlling it? Or reducing it?

The first reason to work to eradicate malaria is an ethical reason - the simple human cost. Every life has equal worth. Sickness and death in Africa are just as awful as sickness and death in America. In Africa and other areas of the developing world, malaria keeps adults from going to work, students from going to school, and children from growing up. Any goal short of eradicating malaria is accepting malaria; it's making peace with malaria; it's rich countries saying:

"We don't need to eradicate malaria around the world as long as we've eliminated malaria in our own countries."  
That's just unacceptable.

If the first reason to eradicate malaria is the human cost, the second reason is the financial cost: If we plan only to control malaria, we will never eradicate it. That means we will keep bearing forever the human costs of malaria, even as we keep paying forever the financial costs of trying to treat and control it. To provide even 80 percent control coverage globally, we will need to spend billions more - each year, every year - than we do today. If, on the other hand, we have a plan to eradicate, we can look toward a time when the human cost of malaria and the financial cost of fighting malaria are both gone for good. In the end, the goal of total eradication is the only way to address the classic problem in disease prevention: how do you ensure that prevention remains a funding priority as you get fewer and fewer cases?

The third reason to go for eradication comes from epidemiology: the ability of the parasite to develop resistance to insecticides and medicines tells us that no set of control strategies can control malaria for very long. Malaria is smart - deadly smart. Fighting it is like playing chess against a computer that changes the rules as soon as it starts losing. This means that without eradication, we will continuously adapt our strategies to the parasite and the parasite will continuously adapt to us - in a back-and-forth battle that will never end.

When I think of what it would mean to eradicate malaria, it brings a memory to mind from a trip I took some years ago to Mozambique. I was visiting a small rural clinic, where I saw a number of children waiting for treatment. One of them, a little girl, was very sick, and the doctors were sending her on to a district hospital, where she could get better care. A physician from our Global Health team was with us. He took a look at the child and said, sadly, that it was a very advanced stage of malaria.

We ended our visit, and I left the clinic. I never learned if that little girl made it to the district hospital, or ever made it home again. It had taken her a long time to get to a doctor. And yet, I couldn't help thinking: she had a better chance than most - because most of the kids with advanced malaria in Africa never even end up in a rural health clinic, much less a district hospital. They die at home with their families - without ever seeing a doctor or getting any treatment.

That is why we have to eradicate malaria. Because little boys and girls in Africa are going to get bitten by mosquitoes. Even if they have bednets, some children will still get bitten when they're out playing at dusk, and some of them are still going to get malaria. And because we can't fix the whole health care system in all of Africa, they're going to die in their village or die on their way to the doctor. No child should die from malaria. No child. And the only way to end death from malaria is to end malaria.

It's fair to ask how is such a thing possible? Is such a thing possible? Here's how we see it. To eradicate malaria, you have to end transmission - and there are multiple points where you can intervene. Reduce the number of infected mosquitoes. Keep mosquitoes from biting people. Keep people who are bitten from getting infected. Keep people who are infected from transmitting malaria back to mosquitoes.

Those are the intervention points. If we could find a tool that was one hundred percent effective, and if we could implement it completely at any one of these points, we would break the cycle of transmission and eradicate the disease. This is just not possible today with the huge numbers of cases and the current tools. But it is possible - using the tools we have today, and addressing all the steps in a multi-pronged approach - to dramatically drive down the number of cases. Then, if we make the cases few enough, and the map of malaria small enough, we could -

theoretically - with a new vaccine, or a new medicine, or a new insecticide - identify and target one step in this cycle, totally stop transmission, and end the disease.

What will that take? If we're going to eradicate malaria, we have to persist and succeed in three crucial areas. We have to take on and solve the complexity of this disease. Conquering malaria is one of the most ambitious medical quests of all time. The resistance to insecticides and drugs means the mosquito and the parasites are moving targets. Winning will take intelligence, agility and speed. Above all, it will take relentless research into vaccines, new medicines, and insecticides by some of the top scientific minds in the world.

We will also have to have tremendous coordination - in every aspect of the effort. This means coordinating research, so different laboratories aren't duplicating the same work and can do research with the benefit of each other's insights. It also means coordinating the work in the field so that we use every tool that we have in the most effective combinations, and no area gets neglected.

Finally, eradicating malaria will take commitment. Not a commitment simply to reduce malaria deaths, or eliminate malaria from certain regions. Those are important milestones - but they are only milestones. A commitment to eradication means a commitment to intensifying the effort as fewer and fewer people get infected. It is counter-intuitive, but absolutely essential.

We understand the risks of declaring a goal of eradication. We understand the mistakes of the past and the obstacles of today. But your work gives us confidence and makes us optimistic. Bill will talk about the promising developments we see - and why we are confident that this generation can succeed where past generations have failed.

Bill?

*Bill Gates:* It's a privilege for Melinda and me to host this conference and see so many people who are doing brilliant work on so many different aspects of this disease. If the parasite were as ingenious as they say, it would target this hall. There is no greater threat to the future of malaria than the energy and intelligence of the people here today. Thank you for coming to Seattle.

What is the most repeated failure in all of global health? It could well be the commitment to eradicate malaria. So why would anyone want to follow a long line of failures by becoming the umpteenth person to declare the goal of eradicating malaria?

There's one reason. We should declare the goal of eradicating malaria because we can eradicate malaria. Today, I want to make the case that we have a real chance to build the partnerships, generate the political will, and develop the scientific breakthroughs we need to end this disease.

My optimism starts with the rush of new actors who are bringing fresh ideas and new energy to the fight against malaria. The biggest players today were not in the game five years ago. The Global Fund for AIDS, TB, and Malaria had just been created. President Bush had not yet announced his major initiative against malaria. Neither had the World Bank. In the past five years, companies like Novartis, GlaxoSmithKline, Exxon Mobil, and Sumitomo have become very involved in the fight. All these groups are now doing more than they've ever done, all at the same time, with a renewed commitment.

The infusion of new money is allowing countries with high rates of malaria to look for the first time at comprehensive, national programs where they can coordinate a wide variety of tools and efforts for maximum effect. No single approach will work alone, but several partially effective approaches can have a huge impact.

Zambia is an inspiring example of a nationally-coordinated effort. Three million long-lasting insecticide-treated bednets are being distributed there this year, and the country is close to reaching its national target of 80 percent of households with at least one net - up from 20 percent two years ago. Any pregnant woman can now get preventive medicines as well as nets for herself and children under 5. And pregnant women at ante-natal clinics in Zambia have reached 62 percent coverage for intermittent preventive therapy - one of the highest levels of coverage in Africa.

Earlier this week, representatives from Zambia and three other countries - Ethiopia, Tanzania, and Mozambique - met together here in Seattle, along with major funders of malaria, to discuss how countries can follow Zambia's model of national scale-up. It is a breakthrough that these countries are considering national programs today; a few short years ago there was only enough funding for district efforts.

This kind of coordination is a huge advance. Medicines, bednets, and insecticides are capable of breaking transmission at the intervention points Melinda talked about. When you use a series of partially effective interventions in combination, they can have a very synergistic effect. For example, the more successful prevention is, the fewer people you need to treat - and the fewer people who are infected, the less chance they can spread malaria to others. So prevention increases the reach of treatment; and treatment is a form of prevention. And they're both much more effective when you coordinate them, which more and more countries are doing today.

I'm also very optimistic because of the extraordinary breadth of research underway - in medicines, vaccines, and other control tools. The transformation in malaria treatment began with the Chinese discovery of plant-based artemisinin and the subsequent developments of artemisinin combination treatments in Southeast Asia, which make it much harder for the parasite to develop resistance. As you know, artemisinin-based combination therapies, or ACTs, are the most effective antimalarial available today. But they're also expensive, supplies are limited, and they require multiple doses over three days. We need to discover new drugs that are not only effective, but also cheap to make and easy to take.

Fortunately, the Medicines for Malaria Venture has the largest and most diverse portfolio of new drug candidates in the history of malaria. One of their most promising projects is an approach to improving on artemisinin with a completely new synthetic peroxide. In early animal studies, a single dose of the synthetic peroxide drug cured malaria - something we've never seen before. This opens the possibility for a single-dose cure of malaria for people. That by itself could transform our fight against the disease.

But that's not all the researchers are up to. MMV and other partners are also making great progress with new plant technology and metabolic fermentation to provide artemisinin at the quantities and savings we need to meet global demand. If you could add those advances to the ability to make the drug synthetically, you could make as much medicine as you need, and far more cheaply and predictably than we do today. These developments could change the world.

Developments in vaccine research today are just as exciting. Researchers with the PATH Malaria Vaccine Initiative are using several different scientific approaches in pursuit of a vaccine. Some are working on a classic approach - which is to pick a few promising antigens and test them. Others are focusing on sporozoites - creating a weakened

form of the parasite that would generate a short-lived infection that would then generate immunity. Yet another group is looking at molecular targets using the latest tools. Never in the history of malaria have so many scientific approaches been used in the pursuit of new vaccines.

In addition to vaccines and medicines, researchers with the Innovative Vector Control Consortium are studying a variety of ways of making mosquitoes less capable of transmitting the parasite. They're also working on new pesticides, to make them more effective in preventing mosquito-borne disease in humans.

I'm also optimistic because we're finding ways to stretch the reach of market forces to get the private sector more involved. GlaxoSmithKline is doing fantastic malaria vaccine research in a way that we hope will become a model for big drug companies. Our foundation pays the cost of the clinical trials; GSK bears the opportunity cost. They're pulling top scientists off of work that could lead to more lucrative discoveries. Since they're not in the business of doing break-even R and D, it's the most you can ask a big company to do and still have any expectation that the CEO will keep his job. It's a terrific model, and I hope it sets a precedent for what private drug companies are willing to do in global health. The benefit to humanity is immense.

In a clear and recent example, the Manhica Health Research Center in Mozambique recently finished a small clinical trial of the world's most advanced malaria vaccine, RTS,S, developed by GlaxoSmithKline Biologicals. This was the first study to test the vaccine in young infants. The trial results - according to a paper published in *The Lancet* today - serve as a proof of concept that the vaccine is safe, is well tolerated, and significantly reduces malaria infection and clinical malaria in infants 10-18 weeks of age. The study reports that vaccine efficacy for new infections was 65 percent over a three-and-a-half-month follow-up period, and that it reduced episodes of clinical malaria by 35 percent during a six-month follow-up from the initial vaccination. These are only interim results, but they are encouraging because they represent a significant step toward fighting malaria infections in an age group most vulnerable to severe illness and death from malaria. There are more Phase 2 studies to be completed, and if all goes well, a large-scale Phase 3 study should begin in 2008 at ten African trial sites.

Melinda and I would like to recognize the many groups that have worked together on this study: the government and people of Mozambique, the hospital clinic at the University of Barcelona, the Spanish Agency for International Cooperation, the PATH Malaria Vaccine Initiative, and GlaxoSmithKline Biologicals.

I want to offer special recognition to Manhica for running the trials. Running a successful trial requires organizing large numbers of trusting people in an infectious area where you know the baseline. When you consider the difficulty, every drug is a miracle drug, just for making it through trials. More than a decade ago, Pedro Alonso - with a grant from the Spanish government and the help of researchers from Mozambique funded by the government - set up Manhica in one of the most malaria-infested parts of Mozambique. I've visited the Center, and it has the health research facilities of a university in a poor, rural setting - and the value to public health is priceless.

Pedro runs a census so he really knows who the kids are and what the baseline is. And he's got the relationship with the community. So researchers don't just wait until they have the vaccines they want to test and say: "okay, let's find a place where we can go get the trust of the community, and figure out the baseline of malaria." He's already done that. It's an extraordinary asset in the search for a vaccine.

We are now working with other committed investigators to expand this approach. Fred Binka and INDEPTH are crucial to this effort. One of their projects, the Malaria Clinical Trials Alliance, is replicating the Manhica effort by working to

strengthen research sites in preparation for what we hope will be Phase 3 trials next year.

These are just some of the reasons why we believe we should declare the goal of eradicating malaria. There is no doubt that if the world dedicates the time and the money, we can develop the tools in the laboratory and coordinate them in the field in a way that will eradicate malaria. The question is - will the citizens and the governments of the world give us that chance?

Right now - in the U.S. government, at the World Bank, we see the approaching end of the funding cycle. Fighting malaria and eradicating malaria is not a short-term job. It's not a four-year or even eight-year event. That can't work in malaria. If you stop halfway, you don't get half the benefit; you could end up with zero percent of the benefit. The progress counts only if we keep it going.

President Bush - by launching the President's Malaria Initiative - has provided a historic level of funding for malaria. If the world is ultimately going to eradicate malaria, then the record funding that began with this president must not end with this presidency. Melinda and I say to every U.S. presidential candidate: if you win this office, you will inherit a record commitment to fighting malaria. The world needs you to sustain it and enhance it. Malaria will never be eradicated without the full support of the president of the United States.

Likewise - the World Bank, under Paul Wolfowitz, has committed record funding to fighting malaria. We call on the new president, Robert Zoellick, to sustain it and enhance it. And the leaders of every developed donor country should generously support the work of the Global Fund, to enhance its role in fighting malaria.

We call on heads of state in countries suffering from malaria to implement a well-coordinated, integrated country-wide program, similar to what's being done in Zambia. And we call on donor countries to step in and help fund these efforts. We call on major donor agencies to work with affected countries to agree on a global plan for malaria - the concrete steps that will make it possible to scale up programs and, ultimately, eradicate the disease. This includes funding, implementation, and monitoring. Then we need those same groups to join together to execute that plan.

In addition, we call on heads of state and heads of foundations and corporations to ensure that as new tools and technologies are developed over the next several years, we can find ways to make them accessible and affordable to those who need them most. Today, we call on world leaders to fund the Affordable Medicines Facility for malaria, a financing mechanism that will provide artemisinin-based combination therapies at reduced prices for those who need them most. ACTs are an incredibly effective treatment for malaria, but their price puts them beyond the reach of most people living in developing countries. If this treatment remains unavailable, people will resort to cheaper, less effective drugs. They may take a form of the drug that will drastically increase the risk of resistance, reducing the effectiveness of this last remaining malaria treatment before the world has time to develop another. We can't let that happen.

We call on the malaria community to press forward with innovation. We have to assess what sets of tools and situations will be necessary to achieve eradication. Then we have to make the investments in innovation necessary to develop the tools and create the situation that makes eradication possible.

Finally - Melinda and I would like to say to the people here in this hall: the hopes of the world rest on you and your colleagues. If you show the world that we can end this disease, you will unleash the energy and the caring and the commitment we need to meet that goal. So keep on fighting, and never lose heart when things go wrong. If one approach fails, take up another.

We're not done, and we will not stop working, until malaria is eradicated. Thank you very much.

**EDITOR'S NOTE:** *Additional information about the malaria forum, including a link to webcasts of key sessions, is available at [http://www.kaisernetwork.org/health\\_cast/hcast\\_index.cfm?display=detail&hc=2288](http://www.kaisernetwork.org/health_cast/hcast_index.cfm?display=detail&hc=2288).*

## "The Global Fund: growing pains"

**Author(s):**

**Reference:** N/A 7(11):695. Editorial.

<http://www.thelancet.com/journals/laninf/article/PIIS1473309907702438/fulltext>

**Published Abstract:** The sound bites and spin coming from the latest replenishment round of the Global Fund to Fight AIDS, Tuberculosis and Malaria have done little to evoke confidence in the Fund's future support. Despite positive press statements from the Global Fund and donor governments at the recent donor replenishment meeting - rather cruelly known as the begging round - in Berlin (Sept 26-28), many governments pledged substantially less than they had previously committed to. But there is no time to brood. Next comes the round 7 meeting (Nov 11-13) where the Global Fund will examine funding proposals for the coming year.

By contrast with the enthusiasm from donors 5 years ago when the Global Fund was founded, the current lack of support is disappointing - and dangerously short sighted. In just a few years, the Global Fund has established itself as the major player in the fight against the "big three" infectious diseases. For example, it currently funds through its grants programme 20% of the HIV programmes in the world, constituting about 60% of its own budget. To date, programmes supported by the Global Fund have provided treatment for 1.1 million people living with HIV/AIDS and 2.8 million people with tuberculosis. According to the Fund's own estimations, these programmes have averted 2 million deaths worldwide. So in light of all this life-saving work, donor apathy is unacceptable.

However, it is easy to be distracted by the Global Fund's financial worries and there are other key factors at play that may limit its effectiveness. Although the Global Fund's remit has always been clear, and its organisational principles are impressive, from its conception the Global Fund was set up as a financial instrument, not an implementation agency. Its aim was to raise and give additional resources for the treatment of HIV/AIDS, tuberculosis, and malaria - according to former UN Secretary General Kofi Annan, it was to be a war chest. The Global Fund would operate transparently and administer funds through a rapid performance-based grant process. Crucially, it would support country-led plans and priorities, form innovative public-private partnerships, and thereby support people and communities living with these diseases. These principles and its focus on the big three has made it unique among international institutions.

Yet despite its best efforts to remain true to its founding principles, the Global Fund has learned through experience that putting these principles into practice is fraught with difficulty. Furthermore, many believe that its tight remit is increasingly becoming a straight jacket. Considerable criticism has been directed at the Global Fund's narrow disease-specific approach by civil society groups and others; an approach which many say distorts comprehensive health planning and diverts resources from other diseases and priorities (for example, other sexually transmitted

infections), and which does not contribute to overall health-system strengthening. In response, the Global Fund implemented a stand-alone grant application process for health-system strengthening in 2005. However, after complaints from donors that this should not be an activity of the Global Fund, rather than fighting its corner, this grant scheme was subsequently stopped. Nevertheless, for the current funding round, guidelines state that applicants can request funds for health-system strengthening if these activities are essential to reducing the impact and spread of HIV/AIDS, tuberculosis, or malaria. This is a welcome step - it shows that the Global Fund is ready to take more of a whole-systems approach that will help make a long and lasting impact on the burden of infectious diseases in resource-poor countries.

Yet there is the opportunity to do more in the seventh round talks and the Global Fund must once again be bold enough to expand its remit. Recommendations made by civil society groups to the Global Fund board have called for institutional support for integrating sexual and reproductive health interventions into HIV/AIDS programmes. The Global Fund has supported very few applications for sexual and reproductive health interventions and has turned down requests for funding for sexual infections other than HIV/AIDS. Several countries have now submitted proposal requests that include such integration. For example, Rwanda has proposed to incorporate gender-based violence, a major driver of the HIV/AIDS pandemic, as an element of its sexual and reproductive health services.

The only sound public health and human rights approach for the Global Fund to take is to start dealing with the wider factors involved in tackling the big three. Expanding its remit to include a greater focus on the wider issues would be the right thing to do. It is time for the Global Fund to rise to the challenge.

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## 7. HIV/AIDS FUNDING

**"Global Fund, World Bank provide Malawi with \$48.5M to expand HIV/AIDS services, Commission says"**

**Date:** 05 November 2007

**Source:** *Kaiser Daily HIV/AIDS Report*

[http://www.kaisernetwork.org/daily\\_reports/rep\\_index.cfm?DR\\_ID=48644](http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=48644)

Malawi's National AIDS Commission in a statement issued Thursday announced that it has received \$48.5 million from the Global Fund To Fight AIDS, Tuberculosis and Malaria and the World Bank to expand HIV/AIDS services in the country up to December, Xinhua News Agency reports. According to NAC, the Global Fund allocated \$44.3 million, while the World Bank provided the remaining \$4.2 million.

NAC said that \$12.5 million has been transferred to UNICEF for the procurement of health products, including antiretroviral drugs and that \$31.8 million will be used to strengthen health systems. According to Xinhua News Agency, the country, with support from the Global Fund, has provided no-cost antiretrovirals to more than 100,000 HIV-positive people since 2005 (Xinhua News Agency, 11/1). Biziwick Mwale, chief of NAC, in July said the country aims to expand the number of people with no-cost drug access to 150,000 by the end of December. He added that the

biggest challenge to increasing access to antiretrovirals is the shortage of health care workers in the country. A recent survey by the Ministry of Health indicates that the country, which has a population of 12 million, employs 150 doctors. According to UNAIDS estimates, there are about 930,000 people living with HIV/AIDS in Malawi, and approximately 78,000 AIDS-related deaths occur each year. The country's HIV prevalence is about 14% (Kaiser Daily HIV/AIDS Report, 7/10).

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## 8. PHARMACEUTICAL INDUSTRY

### "New firm to tackle poor solubility head on"

**Date:** 07 November 2007

**Source:** *in-Pharma Technologist.com*

**Author(s):** Anna Lewcock

<http://www.drugresearcher.com/news/ng.asp?n=81168-formac-pharmaceuticals-drug-delivery-poor-solubility-formulation-oral>

A new Belgian company has joined the throng of pharmas tapping into the booming drug delivery business, but claims that its unique technologies will carve it a place as one of the industry's key players.

Formac Pharmaceuticals, a spin-off company from the University of Leuven, raised \$1.7m to launch its business and plans to distinguish itself by using proprietary oral drug delivery technologies to deal with poorly soluble molecules whilst maintaining drug stability.

While there are many companies riding the drug delivery wave, most focus primarily on controlled release formulations, leaving poorly soluble molecules to be tackled by a much smaller group of firms.

The drug delivery technologies that are currently used to deal with poor solubility essentially revolve around polymer-based systems. However, these technologies tend to result in problems with poor stability, as once molecules are dispersed from a polymer base, they are able to diffuse back into agglomerates causing solubility to drop again.

Thanks to this problem, there are only a handful of drug products on the market using these kinds of systems.

The Formac technologies, however, can deal with poor solubility whilst keeping the stability of the drug at a level that makes it a viable, marketable product, says the company's CEO, Laurens Theunis.

The firm has four proprietary drug delivery technologies, three focussing on immediate release formulations and the fourth on controlled release. The flagship technology is CMO, a silica-based carrier system that accelerates the release of poorly soluble compounds.

Drug molecules are loaded onto the mesoporous silica material, and when the drug-silica matrix enters the gastrointestinal system it attracts water molecules, which then rapidly force the drug molecules out into solution.

Formac plans to use its technology platform in house to develop improved delivery forms of generic products and branded drugs nearing patent expiration, and currently has two products in development due to enter the clinic in mid 2008.

At present, the company is focusing on small molecule drugs, but Theunis revealed that branching into larger molecules may not be so far away, with the firm currently evaluating a new programme not based on small molecule compounds.

However, the company is also providing access to its technologies for external firms to apply to their own drugs in development, and despite only officially launching the company today, Theunis told in-PharmaTechnologist.com that Formac already has contracts with a US "big pharma" and a Belgian company, with a third contract due to be signed today.

"Every pharma company, small or big, always has compounds are put on hold because of solubility," said Theunis.

"Over 40 per cent of the compounds in development are poorly soluble or have some issues with solubility. And that causes a lot of frustration for companies because they're sitting on really potent and selective molecules, but if you can't get them into the body they're kind of useless."

As such, the company believes there is a significant market for its technologies and expertise, and according to Theunis is "convinced" its systems can help solve compound solubility problems.

Despite the increasing prominence of biologic drugs and large molecule therapeutics in pharmaceutical R&D efforts, the quantity of potential drugs sitting on the shelf unused due to solubility issues could provide a previously unavailable revenue stream for pharma firms struggling to fight the onslaught of generic competition and patent expiries.

"Today the market is still based on small molecules and it will be for quite a long time," says Theunis.

"Of course antibodies will be there, and of course proteins will come into the game more and more, but the market for small molecules is still the biggest and the problems there in terms of solubility are huge."

### **"Little room for scientists in pharma's new generation"**

**Date:** 01 November 2007

**Source:** *Financial Times (London)*

**Author(s):** Andrew Jack

[http://www.ft.com/cms/s/0/1e642f10-88aa-11dc-84c9-0000779fd2ac.html?nclick\\_check=1](http://www.ft.com/cms/s/0/1e642f10-88aa-11dc-84c9-0000779fd2ac.html?nclick_check=1)

Andrew Witty is in good company as he gears up to take charge of the world's second largest pharmaceutical group next spring. His recent nomination to head GlaxoSmithKline marks the seventh example in the past two years of a change in chief executive among the world's 10 leading drug-makers.

While each of the handovers has unique aspects, the characteristics of the new generation of pharma leaders - and the way in which they were selected - reveal some common patterns that highlight evolutions and challenges in a sector going through rapid and painful transition.

"This is a tremendously difficult environment," says Jean-Pierre Garnier, the outgoing head of GSK, who describes life for a chief executive in the pharmaceutical sector today as being "in the grinder". "You need energy and resilience. It's not a job for the faint-hearted."

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

### **"Chinese chemicals flow unchecked onto world drug market"**

**Date:** 31 October 2007

**Source:** *The New York Times*

**Author(s):** Walt Bogdanich

<http://www.nytimes.com/2007/10/31/world/asia/31chemical.html?ex=1195016400&en=18904cc9ac3f29c5&ei=5070&emc=eta1>

In January, Honor International Pharmtech was accused of shipping counterfeit drugs into the United States. Even so, the Chinese chemical company - whose motto is "Thinking Much of Honor" - was openly marketing its products in October to thousands of buyers here at the world's biggest trade show for pharmaceutical ingredients.

Other Chinese chemical companies made the journey to the annual show as well, including one manufacturer recently accused by American authorities of supplying steroids to illegal underground labs and another whose representative was arrested at the 2006 trade show for patent violations. Also attending were two exporters owned by China's government that had sold poison mislabeled as a drug ingredient, which killed nearly 200 people and injured countless others in Haiti and in Panama.

Yet another chemical company, Orient Pacific International, reserved an exhibition booth in Milan, but its owner, Kevin Xu, could not attend. He was in a Houston jail on charges of selling counterfeit medicine for schizophrenia, prostate cancer, blood clots and Alzheimer's disease, among other maladies.

While these companies hardly represent all of the nearly 500 Chinese exhibitors, more than from any other country, they do point to a deeper problem: Pharmaceutical ingredients exported from China are often made by chemical companies that are neither certified nor inspected by Chinese drug regulators, The New York Times has found.

Because the chemical companies are not required to meet even minimal drug-manufacturing standards, there is little to stop them from exporting unapproved, adulterated or counterfeit ingredients. The substandard formulations made from those ingredients often end up in pharmacies in developing countries and for sale on the Internet, where more Americans are turning for cheap medicine.

In Milan, The Times identified at least 82 Chinese chemical companies that said they made and exported pharmaceutical ingredients - yet not one was certified by the State Food and Drug Administration in China, records show. Nonetheless, the companies were negotiating deals at the pharmaceutical show, where suppliers wooed customers with live music, wine and vibrating chairs.

One of them was the Wuxi Hexia Chemical Company. When The Times showed Yan Jiangying, a top Chinese drug regulator, a list of 186 products being advertised by the company, including active pharmaceutical ingredients and finished drugs, Ms. Yan said, "This is definitely against the law."

Yet in China, chemical manufacturers that sell drug ingredients fall into a regulatory hole. Pharmaceutical companies are regulated by the food and drug agency. Chemical companies that make products as varied as fertilizer and industrial solvents are overseen by other agencies. The problem arises when chemical companies cross over into drug ingredients. "We have never investigated a chemical company," said Ms. Yan, deputy director of policy and regulation at the State Food and Drug Administration. "We don't have jurisdiction."

China's health officials have known of this regulatory gap since at least the mid-1990s, when a chemical company sold a tainted ingredient that killed nearly 100 children in Haiti. But Chinese regulatory agencies have failed to cooperate to stop chemical companies from exporting drug products.

In 2006, at least 138 Panamanians died or were disabled after another Chinese chemical company sold the same poisonous ingredient, diethylene glycol, which was mixed into cold medicine.

China has an estimated 80,000 chemical companies, and the United States Food and Drug Administration does not know how many sell ingredients used in drugs consumed by Americans.

The Times examined thousands of companies selling products on major business-to-business Internet trading sites and found more than 1,300 chemical companies offering pharmaceutical ingredients. How many others sell drug ingredients but don't advertise this way on the Web is not known.

If the Milan show is any guide, most, if not all, are not certified by China's drug authorities.

China exports drug ingredients to customers in 150 countries, said Sun Dongliang, a Chinese trade official who helped organize his country's Milan exhibitors. Many suppliers have passed inspections by drug authorities and sell active pharmaceutical ingredients, or A.P.I.'s, of high quality, buyers say.

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

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## 9. ANNOUNCEMENTS

## **AVAC - regularly updated Q&A document available**

[http://avac.org/pdf/AVAC\\_draft\\_STEP\\_QA.Nov7.pdf](http://avac.org/pdf/AVAC_draft_STEP_QA.Nov7.pdf)

The AIDS Vaccine Advocacy Coalition (AVAC) has prepared a preliminary question and answer document for advocates to understand the new STEP study data that were made public at the HIV Vaccine Trials Network full group meeting on November 7, 2007. AVAC will continue to expand on and update the analyses in the weeks to come, and urges advocates to refer to the additional documents prepared by trial sponsors [see [http://avac.org/pr\\_step\\_study.htm](http://avac.org/pr_step_study.htm)]. Please send any questions to [avac@avac.org](mailto:avac@avac.org)

## **IOM: Call for Nominations**

New Committee on "The Case for a U.S. Commitment to Global Health: The Sequel to America's Vital Interest in Global Health (1997)."

The Institute of Medicine's Board on Global Health is organizing a 14-month consensus study to examine the case for why the U.S. should make a deeper commitment to global health. The study committee will make evidence-based recommendations that will pertain to the U.S. government, individuals of variable economic means, the private sector, academia, the public health and scientific research communities, the diplomatic and national security communities, foundations, and the media. The committee will also identify key advances, trends, and "lessons learned" since the 1997 America's Vital Interest in Global Health report.

The committee will consist of approximately 12 members (with U.S. and non-U.S. citizenship) with expertise in the following fields: government, international, academic, non-governmental, and industry leadership in medicine and public health; diplomacy; ethics; social sciences; international health care systems and quality; environmental health; international health including chronic and infectious disease, and child survival; global health economics, and epidemiology/public health statistics. Ideal candidates will encompass more than one expertise. The target date for the release of the committee's report in pre-publication form will be February 1, 2009. The project is sponsored by Bill and Melinda Gates Foundation, Burroughs Wellcome Foundation, Fogarty Center of National Institutes of Health, Merck Foundation, Rockefeller Foundation, and U.S. State Department.

Nominations for the study committee should be received by November 16, 2007, to be given full consideration in the appointment process. Recommendations for potential candidates and brief candidate biosketches should be sent to Sarah Scheening, Study Director, at [sscheening@nas.edu](mailto:sscheening@nas.edu).

## **John Shaw Memorial Scholarship to M2008 - Applications Due November 15**

<http://www.aidschicago.org/irmwg/docs/Microsoft%20Word%20-%20The%20John%20Shaw%20Memorial%20Scholarship%20Fund.pdf>

The John Shaw Memorial Scholarship Fund will provide partial scholarships to rectal **microbicides** advocates/members of IRMA for the **Microbicides** 2008 Conference in New Delhi, India, February 24 - 27, 2008.

All scholarships are partial only. Major scholarships are \$US 2,000 and minor scholarships are \$US 500.

*Aims of The John Shaw Memorial Scholarship Fund*

1. To strengthen research literacy and advocacy capacity amongst IRMA membership
2. To promote and enhance the role and standing of IRMA amongst the **microbicide** community
3. To ensure that the knowledge and insights gained at the conference are shared amongst the broader community
4. To facilitate and strengthen IRMA communication and advocacy efforts during the **microbicide** conference
5. To ensure diversity in participation at the conference.

**EDITOR'S NOTE: Please visit <http://www.aidschicago.org/irmwg/docs/Microsoft%20Word%20-%20The%20John%20Shaw%20Memorial%20Scholarship%20Fund.pdf> for applicant criteria and/or to fill out an application.**

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