ALLIANCE FOR MICROBICIDE DEVELOPMENT

28 September 2007, Volume 8, Number 38

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

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

Its purpose is to:

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

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

Areas covered in this News Digest:

1. ALLIANCE UPDATES AND COMMUNITY NEWS

"The honored doctor"
Date: 28 September 2007
Source: *Washington Post*
Author(s): Sue Anne Pressley Montes

http://www.washingtonpost.com/wp-dyn/content/article/2007/09/27/AR2007092701977.html?wpisrc=newsletter

Routinely, his gray Toyota hybrid is parked from 6:30 a.m. until late at night outside Building 31 at the National Institutes of Health in Bethesda. Sometimes his colleagues leave notes on the windshield that say things like, "Go home. You're making me feel guilty."

But Anthony S. Fauci has made a career of long hours, exhaustive research and helping the public understand the health dangers stalking the planet. As director for 23 years of the National Institute of Allergy and Infectious Diseases at NIH, his milieu is the stuff that scares the daylights out of most people: bioterrorism, deadly flu epidemics, the enduring specter of AIDS.

Fauci, who is equally at home in the laboratory, at a patient's bedside, at a congressional hearing or on a Sunday morning talk show, scarcely has time to collect all the accolades that come his way. But this has been an extraordinary year. In the spring, he won the Kober Medal, one of the highest honors bestowed by the Association of American Physicians. In July, President Bush awarded him the National Medal of Science. And today, he receives one of medicine's most prestigious prizes, the $150,000 Mary Woodard Lasker public service award, as "a world-class investigator" who "has spoken eloquently on behalf of medical science," according to the Lasker Foundation.

No one deserves the honors more, his associates agree.

"Dr. Fauci is the best of his kind," said former U.S. surgeon general C. Everett Koop, 90, who has often sought Fauci's medical advice and counts himself as a friend.

For someone else, this might be heady stuff. But Tony Fauci, 66, has never strayed far from his down-to-earth Brooklyn roots or his Jesuit training, with its emphasis on service and intellectual growth. Beginning his career in the lab -- viewed by many as a backwater of medicine -- he soon became the chief detective probing a mystery that would encircle the world. Before AIDS even had a name, he made the "fateful decision," he said, to make it the focus of his research.

"It was a matter of destiny, I think, but by circumstance alone I had been trained in the very disciplines that encompassed this brand-new bizarre disease," he said. "This was in my mind something that was going to be historic."

He and his researchers would make breakthroughs in understanding how HIV, the human immunodeficiency virus, destroys the body's immune system. Years ago, he assumed a public role, calmly explaining the latest health scares on talk shows such as "Face the Nation." Through four presidential administrations, he has led efforts that resulted in Congress dramatically increasing funding to fight AIDS.

Today, as Fauci helps direct the president's emergency plan for AIDS relief in Africa and elsewhere, he also is leading the fight against such infectious diseases as anthrax and tuberculosis. In his $250,000-a-year position, he oversees 1,700 employees and a $4.4 billion annual budget.

"Fauci doesn't sleep," said Gregory K. Folkers, his chief of staff. "He's the hardest-working person you'll ever encounter."

The doctor's curriculum vitae supports that assertion. The bibliography alone is 86 pages, listing 1,118 articles and papers he has written or contributed to. (An example: "The Role of Monocyte/Macrophages and Cytokines in the Pathogenesis of HIV Infection," published in "Pathobiology" in 1992.) He has given more than 2,000 speeches, rehearsing with a stopwatch to whittle down his remarks. He has received 31 honorary doctoral degrees.

Vacations are seldom on the agenda. Often, his wife and three daughters accompany him to events. This summer, it was the International AIDS conference in Sydney. But he is seldom found sitting by the pool behind his Northwest Washington home. And retirement, he said firmly, is "not on the radar screen."

Exceptional Child

He learned to question early. It didn't make sense to him when the nuns at his school said that you had to go to church to get into heaven. His beloved paternal grandfather, an immigrant from Sicily, spent his Sunday mornings cooking. What about him?

"I remember going up to him one day. 'Grandpa, why don't you go to Mass?' And he said: 'Don't worry about it. For me, doing good is my Mass,' " Fauci said. The experience made him determined to do good through his work. He was 7.

The Faucis lived in the Bensonhurst section of Brooklyn, above the family drugstore operated by his father, Stephen, a pharmacist. Fauci's only sibling, Denise Scorce, recalls that he was a well-rounded kid who liked to play ball but only after he did his homework.

"He was very normal in every way, but you kind of knew he was special," said Scorce, 69, a retired teacher who lives in Northern Virginia. "Everything he did was perfect."

Fauci won a full scholarship to Regis High School, a Jesuit institution in Manhattan. Later, he enrolled in another Jesuit school, the College of the Holy Cross in Worcester, Mass.

"The Jesuit training is wonderful. I don't think you can do any better than that," he said. "I always quote, 'Precision of thought, economy of expression.' "

Although he had an aptitude for science, he received his 1962 bachelor's degree in Greek/pre-med. He took the minimum number of science courses required for acceptance at Cornell University Medical College.

"I was very, very heavily influenced by the classics and philosophy, which I think had an important part in my ultimate interest in global issues and public service," he said. "I was interested in broader issues." I always tried to look at things at 40,000 feet as well as down in the trenches."

Encounter With ACT UP

One of the most dramatic episodes during Fauci's tenure at NIH occurred in 1989, when angry ACT UP demonstrators swarmed his building, demanding to be heard. Fauci, like many top government officials, was accused of not doing enough to fight AIDS. The tactics were attention-getting: smoke bombs, staged "die-ins," chalk bodies drawn on

sidewalks.

"He was public enemy number one for a number of years," said writer and activist Larry Kramer, who led the charge. "I called him that in print. I called him very strong, hateful things. . . . But Tony was smart enough to sit down and talk with us."

Fauci read the leaflets the group distributed and others threw away. "If you put it in the context of they were human beings who were afraid of dying and afraid of getting infected and forget the theater, they really did have a point," he said.

When police officers moved to arrest the protesters, Fauci stopped them. He invited a small group to his office to talk.

"He opened the door for us and let us in, and I called him a hero for that," Kramer said in a telephone interview. "He let my people become members of his committees and boards, and he welcomed us at the table. You have to understand that he got a lot of flak for that."

It was worth it, Fauci said. "That was, I think, one of the better things that I've done."

Doctor as Family Man

Christine Grady still laughs when she recalls her first meeting in 1983 with the famous Dr. Fauci. An AIDS nurse who had recently joined the NIH after working in Brazil, she was summoned to interpret for a Brazilian patient who wanted to go home.

Grady was dismayed when the patient responded to Fauci's detailed instructions on aftercare by saying in Portuguese that he intended instead to go out and have a good time. She knew Fauci tolerated no nonsense.

"He said he'll do exactly as you say" is how she translated the patient's remarks.

She thought she had been found out a couple of days later when he asked her to come by his office. Instead of firing her, as she feared, he asked her out to dinner. They were married in May 1985.

The Faucis live in an renovated 1920s home in the Wesley Heights neighborhood. Grady, 55, has a doctorate in philosophy and ethics from Georgetown, and she heads the section on human subjects research at the NIH's Department of Clinical Bioethics. Their children are also busy. Jenny, 21, is a senior at Harvard University; Megan, 18, who will attend Columbia University next fall, does community service teaching in Chicago; Allison, 15, is on the cross-country team at National Cathedral School.

"He's a goofball," said Jenny Fauci of her father. "He works hard and he does his thing, but he comes home and he's singing opera in the kitchen and dancing around."

She thinks she understands what motivates him. "Work is not really work for him," she said. "It's what he believes in."

And so Fauci will leave for the office before dawn and return home long after sunset. It reminds him of that speech he gave this summer at the AIDS conference in Sydney. "It was called 'Much Accomplished, Much Left to Do,' " he said.

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2. MEDIA COVERAGE OF MICROBICIDES

"Saving the world is within our grasp"
Date: 01 October 2007
Source: *Newsweek*
Author(s): Bill Gates

http://www.msnbc.msn.com/id/20920343/site/newsweek/page/0/

Last year my wife, Melinda, and I visited an AIDS clinic in Durban, South Africa. We met women who had walked miles from nearby townships. When they arrived, they were greeted by a well-trained staff. There was an ample supply of antiretroviral drugs, which can help people with AIDS stay healthy for years. Patients were receiving counseling. As we chatted with one of the doctors in the clinic, it struck me: something was fundamentally different.

Nearly a decade ago, when Melinda and I started our foundation, we would go to sub-Saharan Africa or developing countries in other regions and see health workers struggling with broken equipment and empty medicine chests. We walked down dirty hallways packed with exhausted mothers holding sick children. In those days, many took it as inevitable that millions of poor people would die each year from diseases that are preventable, treatable or no longer present in the developed world. But that's starting to change. Today governments, aid groups and communities are simply refusing to accept the notion that diseases like malaria and tuberculosis will haunt us forever. The evidence is in: these problems can be solved.

The world can point to a number of victories already. Smallpox is gone, of course, and polio nearly so. Thanks to the leadership of the Carter Center, we've virtually eliminated guinea-worm disease, an excruciatingly painful parasite that is ingested with tainted water. There are new treatments available for visceral leishmaniasis, also called black fever, which is second only to malaria as the world's deadliest parasitic killer.

Millions of lives have been saved through better financing and delivery of the medical advances available today. The GAVI Alliance has immunized 100 million children, averting some 600,000 deaths last year alone, and a creative approach to the bond markets has raised $1 billion more to buy more vaccines. The Global Fund to Fight AIDS, Tuberculosis and Malaria is saving 3,000 lives a day. That clinic we visited in Durban was made possible by an American program: PEPFAR, the President's Emergency Plan for AIDS Relief. Those lifesaving drugs, the salaries for the staff-even the prefab building-were all financed with American tax dollars.

Some lifesaving solutions can be extremely simple-iodized salt to prevent stunted growth, for example, or oral rehydration solutions to fight diarrhea. Consider that one of the easiest ways to cut down on infant mortality is to keep babies warm and dry. Earlier this year, Save the Children recruited knitters through the Internet to knit and crochet 280,000 caps for infants.

Other solutions will arise from pioneering research now underway. Researchers are hard at work developing vaccines that don't need refrigeration or needles, which could make it easier and cheaper to deliver immunization in poor

countries. Scientists are making important progress on new tools, like **microbicide** gels, to help women protect themselves against HIV. And clinical trials around the world are now testing what may be the greatest scientific breakthroughs of our time: vaccines for malaria, TB and AIDS.

The fight against malaria-which kills a million people a year, mostly children-illustrates how radical thinking can be applied to both discovery and delivery of new interventions. Scientists at Columbia University are trying to block a mosquito's sense of smell so it can't find humans to bite. Others at Virginia Polytechnic Institute are developing pesticides that activate only inside a mosquito, posing no danger to humans or other animals. At the same time, I'm amazed by the work of the Nothing But Nets campaign, which has managed through Web-based marketing to raise $13 million-mostly from young people-for insecticide-treated bed nets.

I believe we stand at a moment of unequaled opportunity. Governments must now step up to the plate with more money-wisely targeted-to expand effective global health programs to reach all those in need. Businesses, community groups and individuals all play a role as well. When Melinda and I visited that PEPFAR clinic in South Africa, we were thrilled to see the progress we've made against one deadly disease. I'm now more convinced than ever that we can create a healthier world for everyone.

"The trials and tribulations of community involvement in research"
Date: 27 September 2007
Source: *PlusNews*

http://www.plusnews.org/report.aspx?ReportID=74528

Francinah Ndala, pastor and chairperson of the township Ladies Forum, is no ordinary member of the community; she is a statuesque woman with a slightly intimidating air, who proclaims that "when I talk, everybody listens". Altogether an ideal candidate to participate in the community advisory group for **microbicide** clinical trials in Soshanguve, a township outside South Africa's capital, Pretoria.

A trial of the **microbicide** gel, Carraguard, is being run by the Population Council, an international non-profit organisation, at three sites in South Africa: the Setshaba Research Centre in Soshanguve, in Cape Town and in KwaZulu-Natal Province.

Microbicides include a range of products - such as gels, films and sponges - that could help prevent the transmission of HIV and other sexually transmitted infections. No **microbicide** has yet been shown to be effective. There are over 20 **microbicide** products in various stages of clinical development in countries including India, Botswana, Tanzania and Malawi.

The community advisory board, which represents communities where the **microbicide** trials are being conducted, is the usual form of local involvement. It acts as a bridge between the community and the research site, provides input into certain components of the trial, and maintains the ethical integrity of the process, according to the Global Campaign for **Microbicides**.

"There was a lot of myths and false information, especially from the ladies that I'm involved with in the community. Some of them were saying Setshaba is offering gel to kill them, which was not true, so I came here to get more information, so that when we are together I can bring the right thing to them," Ndala explained.

Once a month, usually on Friday mornings, the 10 community members on the board meet with the researchers at the Setshaba site to discuss progress in the trial.

Although anybody can be a member of the group, "It depends on how people value you, and whether you have earned their trust. If I come with the information about the trials, I believe they will take it, even though they may criticise and question it at first. At the ultimate end, they will listen to me. They have serious trust [in me]; they believe I cannot lead them astray," Ndala told IRIN/PlusNews.

It is easy to be cynical about how effective "community involvement" in clinical trials really is. Most research into **microbicides** is being conducted in resource-poor countries, in communities hard hit by poverty and HIV/AIDS.

Can untrained and overburdened individuals engage meaningfully with researchers in this highly technical terrain? Or is the process a token gesture, carried out to appear accountable and politically correct?

Tokens or effective intermediaries?

For Dr Khatijah Ahmed, principal investigator with the Carraguard trials in Soshanguve, community involvement is more than just a buzzword. "It's absolutely vital, especially in this field of research, where you're working with HIV, sexual behaviours of people, and there are so many controversies about what works and what doesn't."

She admitted that scientists had been "working in silos" for too long, neglecting the role of communities. "Science cannot function without community involvement; you cannot conduct research in your laboratory and bring people in ... You have to communicate with communities, tell them what you're doing, and make them part of the research from the earliest possible onset."

Before the first trial participants were enrolled, the advisory group in Soshanguve was formed to look at the material used to recruit volunteers and translate it appropriately.

Advisory group member Phillip Langa, who is also an HIV/AIDS counsellor, told IRIN PlusNews that most of the board members see themselves as "ambassadors" of the Setshaba research centre, and their role largely that of informing the community about developments in the trial. "We come here to get the information and then we take it back to our communities."

When asked whether the group would challenge the researchers about results or the trial design, ward councillor Josiah Rabalao said, "We are quite sure the research has no side effects, that's why we have no problem. We are willing to be patient and hear from the doctors."

But this top-down, one-way process made a mockery of community participation, warned Ntokozo Madlala, advocacy officer for the Gender AIDS Forum, a gender lobby group based in KwaZulu-Natal Province.

"They feel that they are employed by the researchers, so the interactions are often biased and there is no aggressive questioning; it's just dictation by the researchers. There should be deliberations," the activist commented.

Staff members at research sites recruit and train the advisory board members, and convene meetings, which could make the members feel that they cannot present conflicting views and should offer answers based on what they think the researchers want to hear.

It does not help that most members have little or no experience in public health, law and ethics or how clinical trials are run, Madlala commented. "The language barrier is a huge problem, and we still have a long way to go in training communities about clinical trials; you can't really engage with these powerful educated people if you don't know enough."

To make matters worse, community advisory boards also tend to get bogged down in the red tape of bureaucracy and the need to reach consensus. In Soshanguve, for example, the Friday meetings can take up the whole morning, and the information about the trials and the training they received has sometimes made them feel that "we were back at school", Ndala said.

Malebo Ratlhagana, community outreach officer at the Soshanguve site, said it has been difficult to get advisory group members to stay the course, as they had had to make a living and were simply volunteers.

Nevertheless, this form of community involvement still has its place. When news broke earlier this year that trials of candidate **microbicide** cellulose sulphate had been stopped after findings that it could increase the risk of HIV infection, Francinah Ndala was kept very busy during her weekly Ladies Forum meetings and church services.

"People were scared; they were hearing a lot of stories and asking me, 'is this your gel that is giving people AIDS?' Some people even stopped using the free condoms from here [Setshaba research site] because they said they [the condoms] also had AIDS. We worked hard to make sure that people knew the right things," she told IRIN/PlusNews.

More meaningful involvement

It has now become generally recognised that community advisory groups on their own play a very limited role, and there has been a gradual shift towards much broader outreach programmes.

In KwaZulu-Natal, for example, the Medical Research Council's HIV Prevention Unit, which oversees a number of **microbicide** trial sites in the province, decided not to have community advisory groups in certain politically charged areas where the forum could "get caught up in different political games and agendas", said Dr Roshini Govinden, principal investigator at the MRC.

Instead, the research site works with municipalities and healthcare workers, and conducts regular community feedback meetings, with smaller meetings at local healthcare facilities and community events.

According to Sinead Delany Moretlwe of the Reproductive Health and HIV Research Unit (RHRU) at the University of Witwatersrand, in Johannesburg, which has been involved in several **microbicide** trials, "the RHRU recognised the importance of wider community engagement some time ago, and has developed a number of strategies to increase community participation in trials".

These include the use of community radio stations and events to make known important health and trial messages, as well as "communicating the results of our own trials to as wide a range as stakeholders as possible ... this approach has helped to build trust within the communities in which we work."

At the end of the year, the results of the Carraguard trial will be announced - the first **microbicide** trial to complete the final stage of testing on humans. Ahmed, a principal investigator, and other researchers at the Setshaba centre are now working with the community advisory group to decide how the results will be disseminated.

Everyone is becoming impatient to know the outcome. "We have explained to people that this goes in stages," Ndala said. "After the trial, researchers must clean up the data and analyse the statistics, so that's why it's taking such a long time. We encourage them to be patient ... even though they are tired and are losing heart."

She is also preparing herself for the outcome: "It's difficult to say I'm excited. We are waiting with bated breath: one part of me is a little bit excited, but the other part ... there is room for disappointment."

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3. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

"Acceptability of tenofovir gel as a vaginal microbicide by US male participants in a Phase I clinical trial (HPTN 050)"
Author(s): Carballo-Dieguez A, Balan IC, Morrow K, et al
Reference: N/A 19(8):1026-31.

http://highwire.stanford.edu/cgi/medline/pmid;17852000

Published Abstract: We studied the acceptability of tenofovir gel among HIV-infected and uninfected men who were exposed to it during vaginal intercourse. The gel was found to be highly acceptable to most men, the large majority indicating they would probably use it in the future if they were concerned about HIV and the product were available. Men liked the gel's transparency and odorless qualities, although reactions to its viscosity were more varied. Men acknowledged women's rights to self-determination concerning HIV-prevention, yet considered that women's covert use of the product was more acceptable in the context of 'one-night-stands' than in stable relationships, for which dialogue on protection measures was preferred. Restrictions to couples' habitual sexual repertoire and the protocol requirement to use condoms resulted in complaints. **Microbicide** trials that do not require condom use from men who don't typically use them may provide a more accurate assessment of acceptability. Consistent **microbicide** use may be contingent on its ease of incorporation into typical sexual practices, type of sexual partnership and contextual issues.

"Desired qualities and hypothetical contextual use of vaginal microbicides in a diverse sample of US women"
Author(s): Olsen ML, Cwiak CA, Koudelka C, et al
Reference: N/A 76(4):314-18.

http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T5P-4PHSFKJ-2&_user=10&_coverDate=10%2F31%2F2007&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=fd682b9d325492344225aaf9f103f5b5

Published Abstract: *Background* Vaginal **microbicides** represent an important emerging class of antiinfectives. To guide research and development, we conducted a survey to determine interest in desired qualities of and intended use of **microbicides** within the current milieu of contraceptive options. *Study Design* Women completed an anonymous survey while waiting for health care clinic appointments in Portland, OR, and Atlanta, GA, and in one public area (Atlanta). *Results* Four hundred one women completed the survey. Subjects had a mean age of 25.6 (SD=7.4), parity of 1.5 (SD=1.6) and 47.7% were non-Caucasian. Respondents showed moderate interest in noncontraceptive anti-HIV gel-based **microbicides** (mean, 53.8; SD, 39.6; n=362) and significantly stronger interest in contraceptive anti-HIV **microbicides** (mean, 89.4 mm; SD, 20.7; n=363; p<.001). The qualities of HIV, pregnancy and sexually transmitted infection (STI) prevention were the highest priorities of the largest percentage (40%) of respondents. Half (49.6%) of respondents reported they would use another form of protection in conjunction with a contraceptive anti-HIV **microbicide**. *Conclusions* A diverse sample of women reported substantial interest in vaginal **microbicides** capable of preventing HIV and pregnancy, and a smaller high-risk subgroup was interested in noncontraceptive anti-HIV **microbicides**. Most women would prefer a product capable of preventing HIV, pregnancy and STIs. Almost half of respondents would use vaginal **microbicides** as part of a dual method.

"Predictors of using a microbicide-like product among adolescent girls"
Author(s): Short MB, Succop PA, Ugueto AM, et al
Reference: N/A 41(4):357-62.

http://highwire.stanford.edu/cgi/medline/pmid;17875461

Published Abstract: BACKGROUND: This study examined demographic, sexual history and weekly contextual variables, and perceptions about **microbicides** as predictors of **microbicide**-like product use. METHODS: Adolescent girls (N = 208; 14-21 years) participated in a 6-month study in which they completed three face-to-face interviews and 24-weekly phone call interviews. Participants were given **microbicide**-like products (vaginal lubricants) and encouraged to use them with condoms when they had intercourse. RESULTS: Of the girls, 75% had had a sexual opportunity to use the product. Using multi-variable logistic regression, the following variables independently predicted ever using the product: length of sexual experience, number of lifetime vaginal partners, and the Comparison to Condoms subscale on the Perceptions of **Microbicides** Scale. Using a mixed model repeated measure linear regression, the following variables independently predicted frequency of use: week of the study, age, condom frequency prior to the study, and three subscales on the Perceptions of **Microbicide** Scale: namely, the Comparison to Condoms subscale, the Negative Effects subscale, and the Pleasure subscale. CONCLUSION: Most girls used the product, including those who were not protecting themselves with condoms. Girls' initial perceptions regarding the product predicted initial use and frequency of use. Further research should evaluate the best methods for supporting the use of these products by young or sexually less experienced girls.

"Seminal plasma reduces the effectiveness of topical polyanionic microbicides"
Author(s): Patel S, Hazrati E, Cheshenko N, et al
Reference: N/A 196Epub ahead of print.

http://www.journals.uchicago.edu/JID/journal/issues/v196n9/38212/brief/38212.abstract.html

Published Abstract: The objective of this study was to test the activity of **microbicides** against herpes simplex virus type 2 (HSV-2) introduced in seminal plasma. We found that seminal plasma interfered with the activity of PRO 2000 and of cellulose sulfate, increasing by 100-fold the concentration of drug required to inhibit 90% of viral plaque formation. Seminal plasma competitively inhibited binding of the **microbicides** to the HSV-2 envelope. Most of the interference was found in a high molecular-weight fraction; tandem mass spectrometry identified the proteins as fibronectin-1 and lactoferrin. In a murine model, the interference translated in vivo into a loss in protection. We found that 2% PRO 2000 gel protected 100% of mice challenged intravaginally with HSV-2 introduced in PBS, whereas only 55% of mice were protected if virus was introduced in seminal plasma (P = .0007, log rank test). If these findings are reflective of what occurs in humans, modifications to **microbicides** to ensure that they retain activity in the presence of seminal plasma are indicated.

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

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4. PUBLISHED RESEARCH: RELEVANT BASIC AND TRANSLATIONAL SCIENCE

"Associations between recent gender-based violence and pregnancy, sexually transmitted infections, condom use practices, and negotiation of sexual practices among HIV-positive women"
Author(s): Lang DL, Salazar L, Wingood GM, et al
Reference: N/A 46(2):216-21.

http://www.jaids.org/pt/re/jaids/abstract.00126334-200710010-00013.htm;jsessionid=G61P5lg1RR4QXfKvs0Y1fdFJ68z3dyHDlQBNwsct4xJDqxhlQ7lR!-2030958118!181195628!8091!-1

Published Abstract: *Background*: This study sought to document the prevalence of recent gender-based violence (rGBV) among seropositive women and to determine the association between rGBV and pregnancy, sexually transmitted infections (STIs), condom use, and negotiation of sexual practices. *Methods*: A total of 304 seropositive women recruited from HIV clinics in the southeastern United States who reported being sexually active in the previous 6 months with 1 partner were included in analyses. Gender-based violence during the previous 3 months, condom use, and negotiation of sexual practices were assessed. Biologic samples for pregnancy and STI testing were collected. *Results*: A total of 10.2% of women reported a history of rGBV. rGBV was related to inconsistent condom use practices, pregnancy, and abuse stemming from requests for condom use. No associations were found between rGBV and negotiation of sexual practices and STIs. *Conclusions*: The prevalence of rGBV among HIV-positive women

emphasizes the need for screening of abuse and highlights the need for the design and implementation of integrated intervention approaches necessary in addressing the needs of this population.

"Potent inhibition of HIV-1 replication by novel non-peptidyl small molecule inhibitors of protease dimerization"
Author(s): Koh Y, Matsumi S, Das D, et al
Reference: N/A 282(39):28709-20.

http://www.jbc.org/cgi/content/abstract/282/39/28709?etoc

Published Abstract: Dimerization of HIV-1 protease subunits is essential for its proteolytic activity, which plays a critical role in HIV-1 replication. Hence, the inhibition of protease dimerization represents a unique target for potential intervention of HIV-1. We developed an intermolecular fluorescence resonance energy transfer-based HIV-1-expression assay employing cyan and yellow fluorescent protein-tagged protease monomers. Using this assay, we identified non-peptidyl small molecule inhibitors of protease dimerization. These inhibitors, including darunavir and two experimental protease inhibitors, blocked protease dimerization at concentrations of as low as 0.01 ÃŽÂ¼M and blocked HIV-1 replication with IC50 values of 0.0002-0.48 ÃŽÂ¼M. These agents also inhibited the proteolytic activity of mature protease. Other approved anti-HIV-1 agents examined except tipranavir, a CCR5 inhibitor, and soluble CD4 failed to block the dimerization event. Once protease monomers dimerize to become mature protease, mature protease is not dissociated by this dimerization inhibition mechanism, suggesting that these agents block dimerization at the nascent stage of protease maturation. The proteolytic activity of mature protease that managed to undergo dimerization despite the presence of these agents is likely to be inhibited by the same agents acting as conventional protease inhibitors. Such a dual inhibition mechanism should lead to highly potent inhibition of HIV-1.

"Rapamycin reduces CCR5 mRNA levels in macaques: potential applications in HIV-1 prevention and treatment"
Author(s): Gilliam BL, Heredia A, Devico A, et al
Reference: N/A 21(15):2108-10.

http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=17885304&dopt=AbstractPlus

Published Abstract: G1 cytostatic drugs reduce CCR5 co-receptor expression and enhance the antiviral activity of a CCR5 antagonist in vitro. The administration of rapamycin, a G1 cytostatic agent, to three cynomolgous macaques led to decreased CCR5 messenger RNA expression in peripheral blood mononuclear cells and cervicovaginal tissue. These results support further clinical evaluation of G1 cytostatic agents such as rapamycin targeting the downregulation of CCR5 expression as a strategy for both the prevention and treatment of HIV infection.

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5. EPIDEMIOLOGY

"Number of HIV cases in Kazakhstan increases, agency says"
Date: 21 September 2007
Source: *Kaiser Daily HIV/AIDS Report*

http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=47655

The number of new HIV cases in Kazakhstan has increased to 1,165 cases in the first six months of 2007, compared with 958 cases reported for the same period in 2006, the Kazakhstan Statistics Agency recently reported, the Times of Central Asia reports.

According to official statistics, 181 new HIV cases were reported in July 2007, compared with 131 cases in July 2006. The increase especially was prominent among children, as 40 new cases of HIV were reported in the July, an increase of 22 cases for the month in 2006. Roza Zhaukimova, an official with the regional administration in South Kazakhstan Oblast, warned that the increase in HIV cases most likely was linked to unsanitary blood transfusions (Times of Central Asia, 9/20).

Although HIV prevalence is low in Central Asia compared with other former Soviet republics, experts have said the region could experience an increase in cases if prevention is not made a priority (Kaiser Daily HIV/AIDS Report, 9/18).

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6. OTHER PREVENTION APPROACHES

"Truck drivers get lesson in safe sex"
Date: 25 September 2007
Source: *China Daily*

http://www.china.org.cn/english/China/225679.htm

A motorcade of more than 20 vehicles took to the highways of Beijing, Hebei and Shandong provinces at the weekend in an attempt to spread the word about safe sex and HIV/AIDS prevention among long-distance lorry drivers. Organized by the China Foundation for Poverty Alleviation, volunteers distributed information leaflets, condoms and syringes at highway service zones and toll stations along the route.

Long-distance truck drivers are generally men in their prime who are sexually active while away from their spouses for extended periods, Hua Ke, the foundation's director, said. "They are highly mobile and often use prostitutes and take drugs, which puts them at risk of contracting the deadly disease," he said. "Worse still, due to poor education and limited access to information, these men know little about HIV/AIDS, let alone how to prevent it," Hua told China Daily.

"That's the reason we targeted them with this project."

Tang Wei, a vice-director of the project, said very few toilets along the highways had posters warning of the risks of HIV, and condoms were often unavailable at service areas. "Starting from next week, all the toilets our motorcade visited will have posters reminding truck drivers of the dangers of HIV and how they can protect themselves from the disease," Tang said.

But the project won't stop there. Over the next five years it will be extended to include key highways across the country, he said. Lorry drivers have been identified as being highly vulnerable to the disease, along with commercial sex workers, homosexual men and intravenous drug users, Hua said.

The Ministry of Health estimates there are 650,000 people with HIV/AIDS, although just 200,000 are registered.

"HIV rise blamed on belief in cure"
Date: 22 September 2007
Source: *BBC News*

http://news.bbc.co.uk/2/hi/health/7007859.stm

A false belief among young HIV patients that the virus can be cured is fuelling a rise in infection levels, a specialist has claimed. Dr Veerakathy Harindra says a quarter of his young HIV patients wrongly believe a cure has already been found. This leads them to fail to take adequate precautions to prevent the spread of the virus, he said. The Terrence Higgins Trust says the number of HIV infections has more than doubled in the last six years.

Dr Harindra, director at Portsmouth's genito-urinary medicine (GUM) clinic, says between 20% and 25% of the young people he sees believe they can be cured of HIV. Drug treatments which help manage HIV have led some people to wrongly believe it can actually be cured altogether, he says.

'Widespread ignorance'

According to the Terrence Higgins Trust, a charity for HIV sufferers, the number of people with the virus has risen from 30,000 in 2001 to 70,000 this year. Research by the charity in July suggested there was still widespread ignorance about HIV, particularly among young people. The poll of 1,000 people found more than 20% of people aged 18 to 24 mistakenly thought there was a cure for HIV. Among the same age group almost a quarter believed condoms had holes in them which let HIV through.

On Friday, international drug company Merck halted trials on an HIV vaccine that was regarded as one of the most promising in the fight against Aids. Merck stopped testing the vaccine after it was judged to be ineffective.

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7. POLITICS AND POLICY

"Report assails F.D.A. oversight of clinical trials"
Date: 28 September 2007
Source: *Washington Post*
Author(s): Gardiner Harris

http://www.nytimes.com/2007/09/28/health/policy/28fda.html?_r=1&hp&oref=slogin

The Food and Drug Administration does very little to ensure the safety of the millions of people who participate in clinical trials, a federal investigator has found.

In a report due to be released Friday, the inspector general of the Department of Health and Human Services, Daniel R. Levinson, said federal health officials did not know how many clinical trials were being conducted, audited fewer than 1 percent of the testing sites and, on the rare occasions when inspectors did appear, generally showed up long after the tests had been completed.

The F.D.A. has 200 inspectors, some of whom audit clinical trials part time, to police an estimated 350,000 testing sites. Even when those inspectors found serious problems in human trials, top drug officials in Washington downgraded their findings 68 percent of the time, the report found. Among the remaining cases, the agency almost never followed up with inspections to determine whether the corrective actions that the agency demanded had occurred, the report found.

"In many ways, rats and mice get greater protection as research subjects in the United States than do humans," said Arthur L. Caplan, chairman of the department of medical ethics at the University of Pennsylvania.

Animal research centers have to register with the federal government, keep track of subject numbers, have unannounced spot inspections and address problems speedily or risk closing, none of which is true in human research, Mr. Caplan said. Because no one collects the data systematically, there is no way to tell how safe the nation's clinical research is or ever has been.

The drug agency oversees just the safety of trials by companies seeking approval to sell drugs or devices. Using an entirely different set of rules, the Office for Human Research Protections oversees trials financed by the federal government. Privately financed noncommercial trials have no federal oversight.

"It's crazy that we have all these different sets of rules," said Dr. Ezekiel J. Emanuel, chairman of the bioethics department at the National Institutes of Health. "It would facilitate things a lot if we had one agency overseeing things."

Dr. Janet Woodcock, chief medical officer at the drug agency, acknowledged that it needs to put more "teeth" in its enforcement. "We are working to address these problems very aggressively," Dr. Woodcock said.

The case of Audine Graybill demonstrates the flaws in the system. According to the F.D.A., in the spring of 2005, she decided to try an experimental drug to treat mania associated with bipolar disorder. The consent form that she signed on May 29 stated that she could change her mind at any point in the study. She checked into High Pointe Healthcare in Oklahoma City, a psychiatric center owned by a psychiatrist, Dr. David Linden. On June 3, Ms. Graybill changed her

mind and asked to leave. Dr. Linden refused to let her go.

On June 6, she was given the experimental medicine. Ms. Graybill's lawyer, Anthony Sykes, obtained a writ of habeas corpus for her to appear in court and took the writ to the hospital, where the staff refused to honor it and said it would not give it to Dr. Linden, Mr. Sykes said.

Mr. Sykes tracked Dr. Linden to another office and had him served with the writ, Mr. Sykes said. Within hours, Dr. Linden's lawyer called Mr. Sykes and said Ms. Graybill was free to go. Mr. Sykes took her home on June 7. Ms. Graybill could not be reached.

More than nine months later, an F.D.A. inspector appeared at Dr. Linden's research center and uncovered myriad other problems. The agency sent its warning letter more than two years after Ms. Graybill's experience.

Last November, the Oklahoma Board of Medical Licensure and Supervision suspended Dr. Linden's license for three months because he had sex with two patients and gave them genital herpes infections, according to board records. Dr. Linden, who also owns a psychiatric center in Las Vegas, did not return repeated telephone messages. Dr. Linden has conducted clinical trials for most major pharmaceutical companies and continues to do research, according to his Web site.

The F.D.A. disqualified investigators from conducting further clinical trials 26 times from 2000 to 2005 and disqualified their data just twice even though the agency found serious problems at trial sites 348 times in that period, the inspector general found.

While some of the report's findings surprised ethicists, its conclusion that the agency's oversight of clinical trials is disorganized and underfinanced has long been known and is, in many ways, identical to criticisms leveled at other agency functions, including its oversight of imported food, foreign drug manufacturers, animal food and the safety of older medicines. In each case, the size and complexity of the tasks facing the agency have grown enormously as the number of inspectors for those tasks has generally declined.

An inspector general's report in 2000 criticized the oversight of clinical trials and noted that the inspections mostly focused on whether study information was accurate and not on whether human subjects were protected. That is still true. In the present report, the inspector general recommended that the agency create a registry of all continuing clinical trials, an idea signed into law by President Bush on Thursday. The report also recommended that the agency create a complete registry of research ethics boards, create a single comprehensive database to track its research inspections and obtain greater authority to regulate research assistants.

Senator Charles E. Grassley, Republican of Iowa, said the agency "needs to implement these recommendations to meet its duty." Representative Rosa DeLauro, Democrat of Connecticut, said it needed more money and guts.

"They're passive, they're reactive, and they often side with industry over public health," Ms. DeLauro said. The agency's reserve is apparent in some of its warning letters.

On May 24, 2005, an inspector, Barbara Breithaupt, went to the office of Dr. Frank A. Wingrove of Ames, Iowa, and for weeks asked to see records of his study of an experimental topical treatment for periodontal disease. Dr. Wingrove refused. Dr. Wingrove did not return telephone messages seeking comment.

More than two years later, the agency sent Dr. Wingrove a warning letter. The inspector general's report suggests that if Dr. Wingrove promised to reform, the agency was unlikely to show up again to see whether he had followed through.

"Bush signs drug safety bill into law"
Date: 27 September 2007
Source: *Associated Press*
Author(s): Andrew Bridges

http://www.washingtonpost.com/wp-dyn/content/article/2007/09/27/AR2007092701109.html?referrer=emailarticle

The Food and Drug Administration on Thursday gained broad new powers to ensure the safety of prescription drugs used by millions of Americans under a bill President Bush signed into law.

At its core, the new law renews for five years programs to collect fees from drug and medical device manufacturers. The industry money accounts for about one-quarter of the FDA's overall budget, defraying the cost of reviewing products that need agency approval.

Members of Congress, acting in the wake of the withdrawal of the painkiller Vioxx three years ago, seized on the bipartisan legislation as a vehicle to reform the FDA's handling of drug safety.

In part, the legislation shifts more of the FDA's attention from experimental drugs pending approval to those already are on the market, and gives the agency more power to act when worrisome problems emerge.

"It really represents an important addition to the FDA's authority," said FDA commissioner Dr. Andrew von Eschenbach.

It gives the FDA the power both to require drug companies to do further study on the safety of medicines, if needed, and to mandate new label warnings when problems do appear. The FDA also gains the ability to fine companies to ensure compliance with those two new authorities. The legislation further requires companies to publicly release results of all clinical trials that show how well their approved drugs performed. Not yet approved drugs could be subject to the requirement later.

Still, how the Food and Drug Administration Amendments Act of 2007 will change the agency remained unclear, beyond the expected hiring of several hundred new employees.

The FDA was still reviewing the 156-page law and its roughly 200 specific provisions, many with timelines, before deciding how to implement them. The fine-print list of actions the FDA must take runs more than 10 pages, said Randall Lutter, the agency's deputy commissioner for policy. The FDA may have to draft new regulations or guidelines - a process that can take years - to implement some of those provisions, Lutter said.

The legislation does spell out that the FDA will be able to fine drug companies for not completing follow-up studies on their drugs after they've won government approval. Those studies frequently remain undone, often leaving important

safety questions unanswered.

The bill calls for drug companies to pay $393 million, and medical device makers $48 million, in various fees next year.

"The increased fees will allow the agency to expand drug safety monitoring, hire additional staff for post-market surveillance, and modernize its information technology systems," said Billy Tauzin, head of the Pharmaceutical Research and Manufacturers of America.

It also requires the FDA to step up its active surveillance for new safety issues with drugs. That system traditionally has been largely passive.

"We welcome the ability to really engage in how those products perform once they are out on the market," said Dr. Janet Woodcock, the FDA's deputy commissioner and chief medical officer, citing the use of data-mining techniques to sift through electronic medical databases for hints of problems.

The manufacturers of certain new drugs will have to draft for each one a so-called "Risk Evaluation and Mitigation Strategy" that can include medication guides distributed with each prescription to ensure the medicine's safe use.

Under the legislation, the FDA will set up a registry to log incidents where adulterated food could pose a health risk. The agency also will have to establish pet food ingredient and processing standards - a provision born of the massive dog and cat food recalls earlier this year.

"It strengthens safety rules for the wave of new miracle drugs coming on the market that Americans count on to protect their health. It brings needed reassurance to families that the food they feed their pets is safe," said Sen. Edward Kennedy, D-Mass.

"PEPFAR programs should focus on sustainable HIV prevention model, experts say at reauthorization hearing"
Date: 27 September 2007
Source: *Kaiser Daily HIV/AIDS Report*

http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=47792

A panel of public health experts on Tuesday at a House Foreign Affairs Committee hearing on the reauthorization of the President's Emergency Plan for AIDS Relief said the program should emphasize HIV prevention that can be sustained in the long term rather than implementing emergency programs, CQ HealthBeat reports (Gensheimer, CQ HealthBeat, 9/26).

PEPFAR directs an authorized $15 billion over five years for HIV/AIDS and tuberculosis primarily to 15 focus countries and provides funding to the Global Fund To Fight AIDS, Tuberculosis and Malaria. PEPFAR's original mandate is scheduled to expire in September 2008. President Bush in May called on Congress to double current funding levels to $30 billion for five years (Kaiser Daily HIV/AIDS Report, 5/31). Joia Stapleton Mukherjee, medical director of Partners in Health, at the hearing said that the $30 billion proposed by Bush is not enough and recommended that the

committee authorize $50 billion over five years for the program. Rep. Nita Lowey (D-N.Y.) last week at a forum on PEPFAR's reauthorization said she is aiming to increase the $30 billion funding level over the next five years. "With these small targets, we are not building," Mukherjee said, adding, "We are simply sustaining work that is less than half done."

Potential Changes to PEPFAR Focus

Foreign Affairs Committee Chair Tom Lantos (D-Calif.) at the hearing said that the "task for the next five years is not only to solidify" the progress PEPFAR has made in its 15 focus countries, "but to reorient the program so that our efforts to combat HIV/AIDS will be sustainable for generations to come." Helene Gayle -- president and CEO of the international development and relief organization CARE, which operates in 11 of PEPFAR's 15 focus countries -- said PEPFAR should work toward creating a sustainable model for HIV prevention. She cited an Institute of Medicine report released in March that recommended PEPFAR transition from focusing on emergency relief to "long-term strategic planning and capacity building." Gayle added that "[a]ddressing HIV/AIDS solely as a medical challenge is like treating the symptoms but not really the cause of the disease."

According to Lantos, PEPFAR should work with focus countries to strengthen health care delivery systems and food security programs. Gayle and Nils Daulaire, president and CEO of the Global Health Council, added that prevention programs would not be fully effective unless funds also support health care systems. Mukherjee added that people in developing countries likely would not travel to clinics to receive an HIV test if the country's health care system is unable to provide treatment.

Rep. Donald Payne (D-N.J.), who chairs the Africa and Global Health Subcommittee, said he believes there is a relationship between PEPFAR's success in focus countries and a concentration on providing adequate nutrition in countries with high HIV prevalence. However, Rep. Ileana Ros-Lehtinen (R-Fla.), the ranking member on the committee, expressed caution about using PEPFAR funds to improve health care systems and establish food security for HIV-positive people. "If PEPFAR is directed to take on the universe of problems that plague the focus countries, we risk reducing it to a program that is a mile wide and an inch deep," Ros-Lehtinen said.

Gayle also recommended that PEPFAR adopt an "ABC-plus" prevention model that incorporates factors not addressed by the program's current ABC model. The ABC model stands for abstinence, be faithful and use condoms. Gayle said that the current ABC model is ineffective for many women in developing countries who are unable to negotiate sex or condom use, adding that the program also should address social, cultural and economic factors that affect girls' vulnerability to HIV.

Some panel members also expressed concern that condom distribution programs have not been effective in the fight against HIV/AIDS. "No generalized HIV epidemic has ever been rolled back by a prevention strategy based primarily on condoms," Norman Hearst, professor of medicine at the University of California-San Francisco, said, adding that successful HIV prevention programs "were achieved not through condoms but by getting people to change their sexual behavior." According to CQ HealthBeat, some of the panelists said that experts have moved beyond the issue of whether one component of ABC is essential for HIV prevention. Daulaire said that successful programs need to focus on "changing social behavior" (CQ HealthBeat, 9/26).

"Shock at archbishop condom claim"
Date: 26 September 2007
Source: *BBC News*

http://news.bbc.co.uk/2/hi/africa/7014335.stm

The head of the Catholic Church in Mozambique has told the BBC he believes some European-made condoms are infected with HIV deliberately. Maputo Archbishop Francisco Chimoio claimed some anti-retroviral drugs were also infected "in order to finish quickly the African people".

The Catholic Church formally opposes any use of condoms, advising fidelity within marriage or sexual abstinence. Aids activists have been angered by the remarks, one calling them "nonsense".

"We've been using condoms for years now, and we still find them safe," prominent Mozambican Aids activist Marcella Mahanjane told the BBC. The UN says anti-retrovirals (ARVs) have proved very effective for treating people with Aids. The drugs are not a cure, but attack the virus on several fronts at once. The BBC's Jose Tembe in the capital, Maputo, says it is estimated that 16.2% of Mozambique's 19m inhabitants are HIV positive. About 500 people are infected every day.

'Serious matter'

Archbishop Chimoio told our reporter that abstention, not condoms, was the best way to fight HIV/Aids. "Condoms are not sure because I know that there are two countries in Europe, they are making condoms with the virus on purpose," he alleged, refusing to name the countries. "They want to finish with the African people. This is the programme. They want to colonise until up to now. If we are not careful we will finish in one century's time."

Aids activists in the country have been shocked by the archbishop's comments.

"Condoms are one of the best ways of getting protection against catching Aids," said Gabe Judas, who runs Tchivirika (Hard Work) - an theatre group that promotes HIV/Aids awareness. "People must use condoms as it's a safe way of having sex without catching Aids," he told the BBC.

Archbishop Chimoio, who made the remarks at celebrations to mark 33 years of independence, said that fighting the disease was a serious matter. "If we are joking with this sickness we will be finished as soon as possible. "If we want to change the situation to face HIV/Aids it's necessary to have a new mentality, if we don't change mentality we'll be finished quickly," he said. "It means marriage, people being faithful to their wives... (and) young people must be abstaining from sexual relations."

Our correspondent says the archbishop is well respected in the country and the Catholic Church played a leading role in sponsoring the 1992 peace deal that ended a 16-year civil war. Some 17.5% of Mozambicans are Catholic.

"The path to new medicines"

Author(s): Callan B, Gillespie I
Reference: N/A 449:164-65.

http://www.nature.com/nature/journal/v449/n7159/full/449164a.html

Published Abstract: Over the next decade, it should be possible to produce a new generation of safe, effective and inexpensive medicines for many of the infectious diseases that afflict the poor. To achieve this, it will first be necessary to address the lack of viable commercial markets, to scale up the global capacity for research and development (R and D), and to build a more efficient and more open mechanism for the discovery of new drugs. Governments can provide the leadership necessary to align the increasingly political issue of global health with philanthropic funding, technological capability and the new opportunities stemming from scientific progress. These are all increasing steadily and now is the time for governments to act.

In June the Organisation for Economic Co-operation and Development (OECD) held a high-level forum on neglected and emerging infectious diseases in Noordwijk, the Netherlands. It brought together senior representatives from government, industry and academia and from philanthropic, international and non-governmental organizations. They discussed how to build strong international support for accelerating the development and delivery of new medicines, vaccines and diagnostic tests for diseases that disproportionally affect developing countries. The consensus that emerged is summarized in the action points of the Noordwijk Medicines Agenda (see box).

Although participants made it clear that many health issues in developing countries will not be solved by new technologies alone, these will still be important for reducing poverty and its consequences. The forum called on governments to show political leadership by joining with industry, product-development partnerships (PDPs), investors, shareholders, and intergovernmental and non-governmental organizations to intensify the cooperation and collaborations that will improve access to new health technologies for infectious diseases.

'Push' and 'pull' tools

Several experiments that include 'push' and 'pull' mechanisms have been introduced since 2000 to spur innovation in the fight against infectious diseases. Push mechanisms increase investment in research at the start of the innovation pathway: for example, by subsidizing the costs incurred when developing products for unprofitable or unpredictable markets. The most promising new push mechanisms involve public-private PDPs, which optimize leads, select candidates and bring products through clinical trials. The dozen or so existing PDPs are mainly funded by philanthropic organizations. Other push tools include basic research funding, targeted R and D funds (such as the proposed Industry R and D Facilitation Fund: http://www.wellcome.ac.uk/assets/wtx026592.pdf) and tax credits.

Pull mechanisms - such as advance market commitments (AMCs), patent extensions, prizes and patent buyouts - are designed to provide incentives for the development and manufacture of usable technologies towards the end of the innovation pathway. They motivate investment by guaranteeing a reward for the product after the completion of its development phase. Pull mechanisms are politically attractive because they address a specific need (for example, lack of a market), are outcome-oriented, and are bounded by time and expense. In theory, pull mechanisms should stimulate a wide variety of discovery efforts in a competitive process but are probably most appropriate when the technological route is marked out. In early 2007, a pilot AMC for the development of a vaccine against pneumococcal disease was launched with a US$1.5-billion commitment by five nations and the Bill and Melinda Gates Foundation,

and a malaria-vaccine AMC is being planned. These funds will subsidize the purchase of a vaccine when it has been developed and is in demand in developing countries.

Designed correctly, a combination of push and pull mechanisms - including subsidies and markets guarantees - could facilitate the development of new vaccines and drugs for neglected diseases. We still do not know what the optimal mix of these policies is likely to be. So it is crucial to establish appropriate metrics for evaluating performance, to understand how to tailor different incentives for a broad range of diseases and treatments.

Open innovation networks

To increase the number of industry and public laboratories involved globally in research into neglected infectious diseases and to maximize the effectiveness of their contributions, a more fundamental transformation of the innovation pathway is necessary. Fortunately, this transformation process has already begun.

Failures in the innovation system can impede the development of appropriate health technologies for the developing world. These can occur at the level of generating and optimizing leads, during the rational identification and selection of candidate drugs from existing compounds, and in the clinical trials used to test new drugs or regimens. In particular, upstream research and early 'proof of concept' work, which provide new leads and create a pipeline of possible new health products, are weak.

The PDPs overcome these barriers by outsourcing knowledge, compounds and tools. The Special Programme for Research and Training in Tropical Diseases (TDR) is one organization that is developing a virtual drug-discovery capacity by using a series of portfolio, screening and medicinal-chemistry networks.

A more open innovation and collaborative research environment would also increase the efficiency and lower the costs of developing new, safe and effective medicines, vaccines and diagnostics through virtual networks (see page 166). What is needed is a better balance between stimulating innovation and providing broader access to knowledge. There are several tools, such as clearing houses and patent pools, and organizational forms, such as networks and consortia, that would promote easier and more open access to elements such as knowledge, data and process innovation. The challenge is to apply these to the neglected infectious diseases. Specific proposals for doing so include creating a shared global portfolio of prioritized drug-discovery projects and a portal for shared drug-discovery tools; matching potential collaborators on a particular project; supplying privileged access to chemogenomics data; and developing common platforms of intellectual property and management-support services.

Intellectual-property rights

The term 'open' applied to innovation does not necessarily mean a freely available source and the absence of intellectual-property protection. The Noordwijk Medicines Agenda recognizes that the protection and use of intellectual-property rights are important for encouraging investment in R and D, but these might not be sufficient to stimulate innovation as far as the neglected and emerging infectious diseases are concerned. But to attract and expand industry participation in such open networks, intellectual-property rights will need to be respected (see page 174), but the norms could be modified within the network. The intellectual property generated by the virtual teams within an open network is likely to be protected as it is in any other public-private collaboration.

Ideally, standard collaboration agreements would facilitate the rapid formation of collaborative arrangements. One possibility is that intellectual-property rights for any successful drug candidates produced would be licensed or donated to the sponsoring PDPs at the start of the clinical-development programme, although rights could be retained

for use in other indications. In short, the network model proposed here is 'open' in the sense that it facilitates broader access to, and use of, data, knowledge and inventions within a worldwide network of researchers, but it would function within the present intellectual-property regime.

Broader innovation benefits

The drug market for infectious diseases in the developing world is both a challenge and an opportunity for the pharmaceutical industry, PDPs and other stakeholders. Unattractive, low-margin markets can be fertile ground for sparking innovation. With lower revenue growth predicted across the pharmaceutical industry in the coming decade, cost containment is becoming an industry-wide problem.

There might be relatively little economic profit to be gained from the development and licensing of drug candidates for the neglected diseases themselves. But there is an economic opportunity in applying the lessons learned from low-cost drug discovery for developing-world diseases to the wider range of niche and segmented non-communicable-disease markets in the developed world. The operation of networks as an emerging model of drug discovery could be an important innovation in its own right.

The top priority in overhauling the innovation system has to be the delivery of medicines for infectious diseases to the poor. Governments can and should use this opportunity to drive a health-innovation strategy that is more efficient and reactive to global public-health needs - one that will leave our innovation systems in better health to deal more effectively with the challenges.

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8. HIV/AIDS FUNDING

"U.N. urges quadrupling of global AIDS spending to meet 2010 treatment goal"
Date: 26 September 2007
Source: *The Washington Post*
Author(s): Craig Timberg

http://www.washingtonpost.com/wp-dyn/content/article/2007/09/25/AR2007092501896.html?wpisrc=newsletter

The United Nations' AIDS agency on Tuesday called for the world to quadruple its spending on the disease in order to reach the U.N. goal of providing universal access to effective treatment by 2010. Agency officials said current spending on AIDS, totaling about $10 billion a year mainly from international donors and the governments of affected nations, would leave two out of three adults who need antiretroviral drugs without them. Efforts to prevent new infections also would fall far below target levels.

"We simply are not spending enough or doing enough," Michel Sidibe, deputy executive director for UNAIDS, said in a conference call with reporters.

The United Nations in 2006 set a goal of providing universal access to treatment, care, support and prevention efforts by 2010. Many nations have endorsed that goal, but even the rapidly growing rate of global AIDS spending is insufficient to meet it, according to a 36-page report due to be issued Wednesday. The report says that spending $42 billion a year by 2010 would allow massive new resources to be deployed, including 427,500 medical personnel and 1.5 million teachers. Bolstered programs would be able to distribute 10 billion condoms and provide 2.5 million circumcisions.

With the extra resources, U.N. officials said, four out of five of those in need of antiretroviral drugs would get them, compared with one in four who get them now. In the report, a level of 82 percent is regarded as universal access because even where services are adequate, not all people with AIDS will use them. The increased spending, officials said, also would halve the number of new infections, though the report does not make clear how this goal would be reached.

Prevention programs have stalled in much of sub-Saharan Africa, the region with the bulk of the world's estimated 40 million HIV infections. The U.N. report recommends using about $150 million a year to improve the availability of circumcision, which recent research has shown reduces the rate of HIV infections by about 60 percent. But the overwhelming majority of the scaled-up prevention spending envisioned by the report would be devoted to strategies that have shown, at best, only modest success in controlling the epidemic in the hardest-hit areas.

Global spending on AIDS has grown by a factor of 30 over the past decade, driven mainly by international donors such as the Bill and Melinda Gates Foundation; the Global Fund to Fight AIDS, Tuberculosis and Malaria; and President Bush's $15 billion anti-AIDS program, which he has proposed doubling. The U.N. report also estimates the cost of an alternative scenario in which universal access to treatment would be reached by 2015 instead of 2010. That would require a tripling of current annual spending levels.

"If we maintain current rates of progress, we are unlikely to achieve universal access by either 2010 or 2015," said Paul DeLay, a top policy official for UNAIDS.

"Agreements signed with USAID"
Date: 24 September 2007
Source: *Agencia de Informacao de Mocambique (Maputo)*

http://allafrica.com/stories/200709241107.html

The Mozambican government and the United States Agency for International Development (USAID) on Monday signed agreements formalising grants of 48.2 million US dollars, out of total development assistance from USAID this year of 157 million dollars in the areas of health, food security, rural incomes, incentives for trade and investment and good governance.

The agreements were signed in Maputo by Mozambican Foreign Minister Alcinda Abreu, the director of the Maputo USAID office, Todd Amani, and the US charge d'affairs, Todd Chapman. The greater part of the US grants for 2007, 95.2 million dollars, are to be used in HIV/AIDS prevention programmes, and in providing care, notably the life prolonging anti-retroviral drugs, to those already infected.

10.4 million dollars have been allocated to mother and child and reproductive health, while a further 18 million dollars will be spent on preventing and treating malaria. 17.6 million dollars has been allocated to food security, and slightly more than seven million in programmes to raise farmers' incomes. A trade and investment programme accounts for 7.8 million dollars. This money is intended to support the private sector, through expanding export industries and developing tourism. Finally, 1.1 million dollars is earmarked to support five municipalities to develop what a US embassy press release calls "a more democratic decision-making process, greater participation by civil society, and efforts to reduce corruption".

The embassy adds that, since 1984, development aid and food aid from the US government, channelled to Mozambique through USAID, has reached 2.083 billion dollars.

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9. ANNOUNCEMENTS

Family Planning: A Global Handbook for Providers

http://www.infoforhealth.org/globalhandbook/

Family Planning: A Global Handbook for Providers, published by the INFO Project at the Johns Hopkins Bloomberg School of Public Health. This handbook, one of the World Health Organization's Family Planning Cornerstones, provides evidence-based guidance developed through worldwide collaboration. It offers clinic-based health care professionals in developing countries the latest guidance on providing contraceptive methods.

EDITOR'S NOTE: To order a print version or dowload a wall chart with text summary, please visit the above website.

Granstmanship Workshop and Mentoring Meetings at M2008

http://2008grantsmanshipworkshop.s-3.net/workshop.aspx

Grantsmanship Workshop For Junior Level and New Investigators February 23, 2008 and Mentoring Meetings February 25-27, 2008 Held in Conjunction with the **Microbicides** 2008 Conference

The objective of the workshop, sponsored by the U.S. National Institutes of Health (NIH), on February 23, 2008, is to provide opportunities for postdoctoral fellows/trainees and investigators to develop grant-writing skills, network with leading HIV/AIDS researchers, and promote collaborations for HIV/AIDS research projects. The workshop will include presentations by NIH staff on the NIH grant-funding processes, tips for writing a successful NIH grant application, pathways for career development, NIH funding mechanisms, and potential sources of funding. A grant review session by a mock Study Section will also be included.

Experts in the field of HIV/AIDS prevention science, including principal investigators from the NIH-funded Centers for AIDS Research (CFAR), as well as representatives from Indian funding agencies, will participate. The experts, who have an interest in collaborating with junior level investigators in India and other nations, will participate in "Meet with Successful Grantees and Experts" sessions to explore possible collaborations. These sessions will be held during lunch breaks on February 25-27, 2008. The involvement of CFAR investigators may provide opportunities for future collaborations that would allow international investigators to use CFAR core facilities, as well as potential consultations in the areas of biostatistics and clinical studies. Alumni of the NIH Fogarty International Center (FIC) and NIH AIDS International Training and Research Program (AITRP) will also be present to share their experiences.

Applications to participate in the Grantsmanship Workshop will be accepted through October 15, 2007.

Upcoming Conferences of Interest

http://www.microbicide.org/microbicideinfo/reference/ConferencesDigest28Sept2007v2.pdf

The Alliance for **Microbicide** Development actively seeks information on conferences of interest for the **microbicide** field and overall HIV and STI prevention community. A monthly updated table will be available on our website with conference titles, locations, and important dates, including early-bird registration and abstract submission. While we recognize that this first table may include conferences that are beyond the abstract/registration dates, the importance of these conferences merits their inclusion. A reminder of this updated table will appear in the last Digest of every month. Please alert Alliance Communications Manager, Latifa Boyce, of any conferences that might also be included, by email: lboyce@**microbicide**.org.

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