



# ALLIANCE FOR MICROBICIDE DEVELOPMENT

**13 April 2007, Volume 8, Number 14**

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 individual articles or complete issues at <http://www.microbicide.org/publications/> and may also search by keyword for articles included in issues of the *Digest* created after 27 January 2006, at <http://www.microbicide.org/publications/search.html>. Should you wish to be removed from the *Digest* distribution list, please advise us at [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

#### "Nigeria: 'Abstinence yet to make impact on HIV/AIDS'"

**Date:** 04 April 2007

**Source:** *Daily Trust*

<http://allafrica.com/stories/200704040444.html>

Abstinence in the advocacy campaign against HIV/AIDS is yet to make the desired impact, Mr Bright Ekweremadu, managing director of Society for Family Health, said yesterday in Abuja.

Ekweremadu in a paper entitled "Prevention of Sexual Transmission of HIV/AIDS in Nigeria" presented at the ongoing National HIV/AIDS Forum said there was little evidence to show that there was a sexual behavioural change among young people resulting from the strategy. To enhance the chances of behavioural change, people, especially young persons, should be provided with other choices and methods of prevention, he added. He said there was need to focus on 'partner reduction messages' in a collaborative manner as it is with abstinence campaign.

Ekweremadu identified difficulty in effecting changes in behaviour, especially among the high risk groups, as one of the major challenges in the fight against HIV/AIDS. He said little focus was placed on reducing sexual partners over the years, despite the social acceptability of such an option. Ekweremadu maintained that young people may find it difficult to abstain, if the approach was not clearly communicated to them, just as recent setbacks in international **microbicides** research posed challenges to the prevention of HIV/AIDS.

Ekweremadu suggested that the focus should be on the high risk group, if the desired impact would be made on the reduction and prevention of HIV/AIDS. He called for open and frank discussions about sexuality and HIV/AIDS infection, especially at the family level.

A resource person at the forum, Dr Abimbola Sowande, called for capacity building on the safe use of injection and appropriate waste management that would aim at promoting behavioural change for health workers. Sowande, who presented a paper on 'Injection Safety', suggested the inclusion of injection safety commodities in federal government's essential drug list.

In their paper 'HIV/AIDS Counselling and Testing, (reaching more to reap benefits)", Dr. Emmanuel Isamade and Rosemary Nnamdi-Okagbue said the federal government's aim of treating 250,000 people living positively (PLP) may not be actualized because of inadequate number of trained counsellors. The number of health facilities providing anti-retro viral therapy (ART) and referral system is in short supply in the country, they observed. They said the issue of stigma would remain a challenge as there was no community, family and partner support. To that end, they advocated for the integration of HIV/AIDS counselling and testing into the primary health care system. They suggested the coordination of multi-sectoral approaches at national, state and local government levels.

The coordinator of the National Blood Transfusion Service, Dr. Folake Ayo, in her presentation, said 'blood transfusion holds a major entry point for HIV/AIDS'. She said the only way to avoid this trend was to set up a national blood screening policy and engage in campaign for the formation of more blood donor clubs in the country.

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## 2. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

### "Practice Brief: Adolescents and HIV clinical trials: Ethics, culture, and context"

**Author(s):** Macqueen KM, Karim QA

**Reference:** N/A 18(2):78-82.

**Published Abstract:** One quarter of HIV infections globally occur among young people 15 to 24 years of age, and more than half of all new infections are in people younger than 25 years. Clearly, there is a need to identify and implement effective HIV prevention strategies among at-risk teens. Some of the most effective options for slowing the epidemic are biomedical, and several promising methods are in development, including **microbicides**, vaccines, and preexposure prophylaxis (PREP, or the daily use of antiretrovirals to prevent the acquisition of HIV). There is widespread reluctance to enroll minors in such biomedical prevention trials because of concerns about vulnerability related to physical maturity, experiential maturity, and diminished autonomy as well as legal and social challenges that vary across and within nations. However, excluding minors from trials misses an important opportunity to evaluate the effectiveness, acceptability, and safety of innovative interventions under the best conditions for identifying and resolving potential problems. The challenges of including minors in HIV prevention trials are highlighted through the example of one rural South African community that has been particularly devastated by the HIV epidemic.

### "Protein design of a bacterially expressed HIV-1 gp41 fusion inhibitor"

**Author(s):** Deng Y, Zheng Q, Ketas TJ, et al

**Reference:** N/A 46(14):4360-9.

**Published Abstract:** Peptides derived from the carboxyl-terminal heptad repeat of the gp41 envelope glycoprotein ectodomain (C-peptides) can inhibit HIV-1 membrane fusion by binding to the amino-terminal trimeric coiled coil of the same protein. The fusion inhibitory peptide T-20 contains an additional tryptophan-rich sequence motif whose binding site extends beyond the gp41 coiled-coil region yet provides the key determinant of inhibitory activity in T-20. Here we report the design of a recombinant peptide inhibitor (called C52L) that includes both the C-peptide and tryptophan-rich regions. By calorimetry, C52L binds to a peptide mimic of the amino-terminal coiled coil with a  $K_d$  of 80 nM, reflecting the large degree of helicity in C52L as measured by circular dichroism spectroscopy. The C52L peptide potently inhibits *in vitro* infection of human T cells by diverse primary HIV-1 isolates irrespective of coreceptor preference, with nanomolar  $IC_{50}$  values. Significantly, C52L is fully active against T-20-resistant variants in a single-cycle HIV-1 infectivity assay. Moreover, because it can be expressed in bacteria, the C52L peptide might be more economical to manufacture on a large scale than T-20-like peptides produced by chemical synthesis. Hence the C52L fusion inhibitor may find a practical application, for example as a vaginal or rectal **microbicide** to prevent HIV-1 infection in the developing world.

### "Rectal microbicide acceptability: results of a volume escalation trial"

**Author(s):** Carballo-Diequez A, Exner T, Dolezal C, et al

**Reference:** N/A 34(4):224-9.

**Published Abstract:** **OBJECTIVES:** The objectives of this study were to determine what volume of a **microbicide** placebo gel is acceptable when applied intrarectally before receptive anal intercourse (RAI); and to evaluate responses to properties of the gel, its application, and its use. **STUDY DESIGN:** HIV-uninfected men who reported unprotected RAI with serodiscordant or unknown-status partners were enrolled in a volume escalation trial. **RESULTS:** Up to 35 mL of gel with the physical properties of Femglide (transparent and odorless) was acceptable to the majority of participants. Choice of different levels of viscosity may be needed. For some men, volumes judged acceptable when tried without intercourse were not acceptable when used during sex. Overall, participants reported high intentions to use **microbicides** when available. Condom use was inconsistent despite advice to use condoms. **CONCLUSIONS: Microbicides** that would require up to 35 mL of volume to be effective would be acceptable to men who engage in high-risk RAI.

### "Synergistic inhibition of HIV-1 infection by combinations of soluble polyanions with other potential microbicides"

**Author(s):** Gantlett KE, Weber JN, Sattentau QJ

**Reference:** N/A Epub ahead of print.

**Published Abstract:** Several polyanionic compounds with potential for use as topically applied **microbicides** to prevent HIV-1 sexual transmission, such as PRO 2000, are currently in phase III clinical efficacy trials. **Microbicial** formulations may well comprise combinations of inhibitors to increase potency, reduce dose and minimize problems of HIV-1 resistance. We have therefore evaluated *in vitro*, the anti-HIV-1 activity of two leading polyanionic **microbicides** combined with other antiretroviral agents with **microbicial** potential. Dextran sulfate (DS) and PRO 2000 were combined with the neutralizing antibody IgG1b12, the peptide-based fusion inhibitor T20, the CCR5 antagonist

TAK779 and the cyanobacterial protein cyanovirin-N. Anti-HIV-1 activity was assessed in a single cycle replication assay using pseudoviruses carrying a luciferase reporter gene and the envelope glycoproteins from HIV-1 isolates JR-FL (R5) and HxB2 (X4), against both immortalized and primary CD4+ cell targets. The data were analyzed for synergy using Calcusyntrade mark software. Results indicate that PRO 2000 and DS can act synergistically with most inhibitors tested, although the degree of synergy depends on inhibitor concentration and combination. These data provide a rational basis for testing of **microbicide** combinations *in vivo*.

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

#### "Synthesis and anti-HIV-1 activity evaluation of 5-alkyl-2-alkylthio-6-(arylcarbonyl or alpha-cyanoarylmethyl)-3,4-dihydropyrimidin-4(3H)-ones as novel non-nucleoside HIV-1 reverse transcriptase inhibitors"

**Author(s):** Ji L, Chen FE, Clercq ED, et al

**Reference:** N/A 50(8):1778-86.

**Published Abstract:** A series of novel S-DABO analogues (S-DABOs, 1) were synthesized and evaluated as inhibitors of human immunodeficiency virus type-1 (HIV-1). Key structural modifications included replacement of the 6-arylmethyl group by a 6-arylcarbonyl or 6-(alpha-cyanoarylmethyl) group. Most of the compounds showed only micromolar potency against HIV-1 in MT-4 cells *in vitro*, though two of them (3e and 3g) were unusually potent (IC<sub>50</sub> = 0.09 and 0.002 μM, respectively) and selective (SI = 1500 and 4600, respectively). Structure-activity relationships among the newly synthesized S-DABOs are discussed.

#### "U.S. women's one-year contraceptive use patterns, 2004"

**Author(s):** Frost JJ, Singh S, Finer LB

**Reference:** N/A 39(1):48-55.

**Published Abstract:** CONTEXT: Unintended pregnancies occur far too often in the United States, and half occur when couples fail to practice contraception. Improved measures of the continuity of women's contraceptive use, nonuse and switching patterns can help identify ways to reduce unintended pregnancy. METHODS: A nationally representative sample of 1,978 adult women at risk of unintended pregnancy was surveyed by telephone in 2004. Respondents provided detailed information about contraceptive use and periods of stopping or switching methods during the past year. A typology of patterns of contraceptive use was created, classifying women into mutually exclusive categories according to their exposure to pregnancy risk. RESULTS: Twenty-three percent of women at risk of unintended pregnancy were exposed to a high risk of pregnancy because of gaps in contraceptive method use in the year prior to the survey-8% were consistent nonusers, and 15% experienced 1-11 months of nonuse while at risk. More than half of women used a method during each of the previous 12 months-38% used the same method or methods all year, and 24% switched methods. Fifteen percent of women had gaps in contraceptive use when they were not at risk. Women reported a variety of reasons for their gaps in contraceptive use, including method-related

difficulties and side effects, infrequent sex and being ambivalent about avoiding pregnancy. CONCLUSIONS: Strategies for reducing gaps in contraceptive use include improved counseling to help women both choose the right method and continue method use, especially when they have periods of infrequent sexual activity or are experiencing method-related side effects or problems.

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#### 4. POLITICS AND POLICY

##### **"Africa plans to produce own drugs, reduce reliance on West"**

**Date:** 11 April 2007

**Source:** *Agence France Presse*

<http://www.africasia.com/services/news/newsitem.php?area=africa&item=070411134853.lsk6rnou.php>

Africa is gearing up to produce its own essential drugs, reducing reliance on the West for lifesaving medicines for disease such as malaria and tuberculosis, the African Union said Wednesday. A plan detailing options for the continent to produce cheap, quality generic drugs for those in need would be presented to health ministers attending a conference in Johannesburg.

"We need to produce (medicines) in Africa. We have the potential, why do we want to take them from outside when we can take it in Africa?" Mamadou Diallo, chief pharmacist in the AU commission's medical services directorate, told AFP. "The main objective is to identify which kinds of medicines we are going to produce, essential drugs we need for Africa, and who is going to produce these drugs."

Many African countries currently rely on India and China for imports of affordable generic drugs, but both countries are subject to patent laws which threaten Africa's access to the medicines. According to Diallo, Africa has all the resources and capacity at its disposal to manufacture essential medicines for the opportunistic infections like tuberculosis, malaria and HIV/AIDS which plague the continent. Egypt has more than 30 drug manufacturing plants, Nigeria and South Africa already produce medicines and a World Health Organization (WHO) assessment showed that out of 46 countries, 37 had pharmaceutical industries. "All the resources are already available. Since those manufacturing plants are already in place, there is already the capacity to run them. The manpower to run that plant is already there," said Diallo. He said it would be up to the respective health ministers at the conference to take the plan forward.

Nthari Matsau, deputy director general in South Africa's health ministry, confirmed that the respective ministers would be discussing the pharmaceuticals plan but refused to give further details until after the meeting.

##### **"U.S. HIV/AIDS efforts should shift focus to sustainability"**

**Date:** 01 April 2007

**Source:** *Kansas City infoZine*

<http://www.fozine.com/news/stories/op/storiesView/sid/21959/>

While the U.S. government's global HIV/AIDS relief program is making significant contributions to addressing the pandemic in hard-hit countries, continued support and increased flexibility are needed to achieve lasting impact against the disease, says a new congressionally mandated report from the Institute of Medicine and the National Research Council. It evaluates the progress of the President's Emergency Plan for AIDS Relief (PEPFAR) and recommends that the program shift its primary focus from providing immediate, emergency relief to building the capacity of affected nations to sustain their fight against HIV/AIDS over future decades. That shift should include expansion and better integration of prevention, treatment, and care services for all at-risk populations; increased attention to factors that raise the vulnerability of women and girls; and greater emphasis on ensuring that U.S.-sponsored activities are in tune with other anti-HIV initiatives in each country, the report says.

In particular, prevention efforts should be intensified to help keep rising infection rates from overwhelming the capacity of the program's partner nations to provide treatment and care, added the committee that wrote the report. PEPFAR has not always supported the most appropriate mix of prevention strategies to fit each country's circumstances, the committee said, in part because congressional mandates have directed how PEPFAR funds must be allocated. Because flexibility is crucial to successful response efforts, Congress should eliminate these restrictions and instead use mechanisms that would give countries greater latitude in directing resources while also ensuring that they meet performance targets for prevention, treatment, and care.

"In its first two years, PEPFAR has demonstrated what many doubted could be done, namely that HIV/AIDS services can be scaled up rapidly in countries with severe resource constraints and other daunting obstacles," said committee chair Jaime Sepulveda, Presidential Chair and visiting professor, University of California, San Francisco. "These accomplishments are just a start, however. For continued progress toward PEPFAR's five-year targets and ultimate goals, U.S. efforts should transition from focusing on emergency relief to long-term strategic planning and capacity building. And they should ensure that countries can direct resources where they are needed most."

The report's recommendations for improving PEPFAR are based on the presumption that Congress will reauthorize legislation to continue U.S. efforts to provide global AIDS assistance. PEPFAR grew out of legislation passed in 2003 that authorized \$15 billion for HIV/AIDS-related relief to be disbursed over five years through a strategy outlined by the president.

PEPFAR's five-year timeframe has raised concerns about whether the countries receiving its aid will be able to sustain their programs without continued support. However, the Office of the U.S. Global AIDS Coordinator (OGAC), which oversees PEPFAR, has declared "building capacity for sustainable, effective, and widespread HIV/AIDS responses" to be one of the program's cornerstones. OGAC should continue to focus on planning for the next decade of U.S. efforts to fight AIDS globally, the committee urged.

Intensifying evidence-based prevention activities will be critical for long-term success, the report says. PEPFAR aims to prevent at least 7 million HIV infections in 15 focus countries by 2010. OGAC reports that millions of people have received various prevention services with PEPFAR assistance, but it is not yet clear how many infections these efforts ultimately will avert.

PEPFAR's prevention planning is controlled in part by budget allocations mandated by Congress, which require that 55 percent of PEPFAR funds go to treatment, 15 percent to palliative care, and 10 percent to assist children affected by the epidemic, leaving 20 percent for prevention. In addition, Congress mandated that at least 33 percent of the prevention funds be directed to programs that promote abstinence until marriage. But HIV infection patterns vary among countries, some of which have relatively high rates of mother-to-child transmission, while others have higher rates of infection acquired via injection drug use.

The budget mandates may have been helpful initially in ensuring that attention would be given to all aspects of HIV/AIDS response - prevention, treatment, and care - and that needs such as caring for orphans would not be neglected. But the mandates are impeding the fully effective use of funds, the committee concluded. PEPFAR teams in the focus countries report having difficulty targeting sufficient resources and interventions to those at greatest risk of acquiring HIV. The budget mandates do not guarantee that the resources and attention being given to treatment and care strategies will yield the greatest impact, either. Inflexibility also hampers the program's ability to lead the way in using innovative techniques as they are validated and become available, the report concludes.

Another PEPFAR policy that has impeded the program's ability to harmonize its efforts with partner countries' other initiatives against HIV/AIDS is the requirement that all antiretroviral medications purchased with PEPFAR funds be approved by the U.S. Food and Drug Administration. Although the goal is to assure the quality of the drugs, most of the focus countries and other donors rely on the World Health Organization (WHO) Prequalification of Medications Project for quality assurance. Many of the generic antiretroviral drugs used in recipient countries have since been FDA-approved for purchase through PEPFAR. In the future, however, OGAC should work to support WHO prequalification as the accepted global standard for quality assurance.

PEPFAR's strategy has been responsive to Congress' desire that the program help address the particular vulnerability of women and girls. In the transition from emergency relief to a sustained commitment, the U.S. Global AIDS Initiative will need to keep gender issues at the core of its efforts. It should support improvements in the legal, economic, educational, and social status of women and girls.

The report was sponsored by the U.S. Department of State. Established in 1970 under the charter of the National Academy of Sciences, the Institute of Medicine provides independent, objective, evidence-based advice to policymakers, health professionals, the private sector, and the public. The National Research Council is the principal operating agency of the National Academy of Sciences and National Academy of Engineering. A committee roster follows.

Pre-publication copies of PEPFAR Implementation: Progress and Promise are available from the National Academies Press; tel. 202-334-3313 or 1-800-624-6242 or on the Internet at <http://www.nap.edu>. In addition, a podcast of the public briefing held to release this report is available at <http://national-academies.org/podcast>.

## **"Bringing cancer science to the bedside"**

**Source:** *The Scientist*, Volume 21, Issue 4

**Author(s):** Edyta Zielinska

<http://www.the-scientist.com/article/home/52976/>

Craig Jordan began studying cancer stem cells in 1998, when it was still a relatively new field. He soon realized that most drug developers weren't taking advantage of this new science, and he started looking into ways to specifically target leukemic stem cells. His big break came when he discovered that the transcription factor, nuclear factor kappa B (NFkB), was overexpressed in the stem cells because there was already a known agent that inhibited it: parthenolide. "But that was just the beginning," says Jordan. For the next five years he and his team developed and tested analogs of parthenolide that were soluble and would actively kill stem cells. One of the two agents his team found is scheduled to go into Phase I trials this year. "It's a little scary but really exciting," says Jordan. "We won't really know if it works until it goes into humans."

The National Institutes of Health wants this scenario to occur more often. In October 2006, NIH committed \$100 million to help build infrastructure for 12 translational (bench-to-bedside) research centers around the country, and pharmaceutical companies are following suit. These programs are looking for qualified scientists to bring onboard. Another major focus of the grant - and an area of opportunity for researchers - is on the training programs that each center is required to develop. Scientists and medical doctors will be able to train quickly on clinical research and regulatory requirements and fill what many translational cancer researchers see as a shortage of well-trained researchers.

The centers won't only focus on cancer research, since NIH wants to increase translational research across all disciplines. However, cancer researchers such as Jordan hope the grant will help make translational work easier by helping to organize and provide the logistic support for clinical trials.

Many academic centers have spent the last few years preparing to increase their translational cancer work, which would shift some of the early work of drug testing from biotech and pharma companies to academic campuses. Such work includes developing and then manufacturing a compound or agent, testing it for toxicity in animals, and then carrying out early clinical trials. For example, the University of Pennsylvania introduced three new core facilities at the Abramson Cancer Center to provide support for translational research: a GMP (good manufacturing practice)-qualified manufacturing facility to produce experimental drugs, a cellular immunology testing facility that processes patient samples and conducts the GLP (good laboratory practice)-qualified assays, and an office that helps researchers prepare the regulation-heavy applications for investigational new drugs. Carl June, head of the program, says he's already found 60 non-cancer researchers at the University of Pennsylvania who are interested in translational work and who will need his center's support.

By 2012, NIH plans to have 60 translational research centers operational. They will act as a consortium, enabling others to share and adopt the best ideas and methods. NIH had planned to give only seven awards the first year, but it was so impressed with the applicants that instead, 12 were granted. They include: Columbia University Health Sciences, Duke University, Mayo Clinic College of Medicine, Oregon Health & Science University, the Rockefeller University, University of California, Davis, UC, San Francisco, University of Pennsylvania, University of Pittsburgh, University of Rochester, University of Texas Health Science Center at Houston, and Yale University.

The new centers will help unite researchers and clinicians, who rarely interact but must do so for translational medicine to work. "Scientists and physicians really live in different worlds and speak different languages. It's difficult to create an environment where scientists and physicians can work effectively," Jordan says. He heads the Wilmot

Cancer Center at Rochester, which is constructing a building to house both labs and inpatient facilities so that scientists and physicians can interact on a regular basis. Jonathan Pollett, a postdoc at Pittsburgh, has worked on clinical trials for his doctorate and is trying to improve cancer models. He says working with clinicians is key to his success: "If you don't interact [with physicians] and learn what they need to figure out, it's like building bridges from two ends of a stream and hoping they meet in the middle."

Pharmaceutical companies are also gearing up for more translational medicine. Robert Abraham, vice president of Wyeth's oncology discovery group, says translational medicine is one area that is going to produce "quantum leaps" in drug development, especially in the cancer arena. "Due in large part to the war on cancer for the past 25 years, there's been very intensive effort to dissect the molecular events that lead to cancer development," says Abraham. These advances have led to therapies that target a molecule or oncogenic pathway rather than a cancer subtype. Finding out "who's most likely to respond to the molecularly targeted drugs [across cancer subtypes]," is possible today, says Abraham, with biomarkers that identify patients who will respond to a specific drug.

Wyeth reorganized its translational research efforts in 2006. Gerald Burr, vice president of scientific communications, says that other companies are aggressively recruiting many of the nearly 100 Wyeth scientists who have expertise in translational medicine.

#### *New opportunities*

For Preet Chaudhary, the biggest problem in translational research is the lack of qualified personnel. Chaudhary, who directs the center for translational research at Pittsburgh, says he needs people at all levels who understand what is needed to develop a drug for humans, especially the importance of regulatory requirements. When the principal investigator needs to spend too much time explaining the regulatory concerns, Chaudhary says, it can detract from effective management of the trial.

Translational research in cancer is growing. Just in the past five years, Pittsburgh's cancer institute has hired around 51 researchers to do translational work, "each of which brought anywhere from three to 17 people with them," says Clair Collins, assistant director of the news bureau at Pittsburgh's medical center. In general, institutions need more investigators who are trained in both science and medicine and can grasp translational work and drug development, says David Warner, associate director of the Mayo Clinic's NIH-funded translational program. "It's been recognized in the past several years that we're losing our ability to do good quantities of high-quality clinical research," says Warner.

NIH is making it easier for scientists who are interested in translational research but lack the experience. As a requirement for receiving NIH's Clinical and Translational Science Awards, institutions must create formal training and degree programs for its scientists and clinicians to get up to speed on clinical trials. "Institutions will [soon] be providing this type of clinical research education and an expanded menu of options," from full-fledged PhD degrees to an MS for medical doctors and researchers, as well as certificate programs that offer fast-track courses in drug development, says Warner.

Until now scientists and physicians relied on individual career-development NIH grants that allow them to take time off their degrees to learn about clinical research. Jennifer Grandis, an otolaryngologist at the University of Pittsburgh, took a year off towards the end of her residency to do research in a molecular biologist's lab at the cancer center. "After I became competent in doing the surgery, I thought, 'this isn't enough,'" she says. "I wanted to understand how to prevent these tumors." She sees patients one day per week and does surgery one day per week, but the rest of her

time is devoted to clinical research. She expects to start a Phase I trial of a new compound later this year.

"[These degrees are] going to be the future," says Paul LaCelle at Rochester University. "A PhD in genetics [alone] won't be all that sought after." The master's program at Rochester is starting small, taking four graduate students per year and two PhD students. They expect the PhD program will be approved this summer.

Chaudhary hopes to retain in his own labs some of the students trained through Pittsburgh's programs. He says he looks forward to working with excellent cancer researchers who are well versed in the intricacies of clinical trial protocols.

#### *Ongoing concerns*

Some scientists say they shy away from translational cancer work, fearing they'll get lost in the crowd of investigators needed to bring a drug to the clinic. Researchers typically measure their progress by the number of publications to their name, but clinical trials often take more time to plan and execute than other projects, which limits the number of studies in which scientists can participate. And with many coauthors, individual scientists share a smaller slice of "glory pie" when involved in a set of significant findings. "There has been a lot of resistance by researchers to shift resources from basic [science] to do clinical science," says Francesco Marincola, editor in chief of the *Journal of Translational Medicine*. Warner expects that to change when translational research is made into a distinct academic discipline through the specialized degree programs.

Some institutions aren't waiting for the reputation of these programs to trickle down. At the Abramson Cancer Center, June says many at his institute are starting to think about how to promote clinical researchers who will have fewer publications to show for their efforts. "It's a national issue," he says. "We're going to have to learn how to promote people like this. [Translational research] is a new specialty."

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## 5. PHARMACEUTICAL INDUSTRY

### "Gilead shifts Irish ops"

**Date:** 12 April 2007

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

**Author(s):** Anna Lewcock

<http://in-pharmatechnologist.com/news/ng.asp?id=75685>

Major biopharma Gilead Sciences has announced plans to invest in a new €60m plant in west Dublin, Ireland, to expand manufacturing capacity and meet future growth targets. The new facility will house activities previously carried out at the firm's other Dublin site, which has reached maximum capacity and is no longer able to meet manufacturing requirements.

Formal planning application for the 20-acre site with 200,000 sq. ft of buildings will be submitted by the end of this month, with construction due to be completed by the end of 2008 and operations anticipated to begin in early 2009. The new plant will have a fill and finish facility along with other logistical and warehousing support structures,

and will also have space to accommodate future expansion plans involving a new tableting facility. Plans for the old site have yet to be formally decided, but it is situated on the Sandyford Industrial Estate south of Dublin which is a highly sought after patch, already housing the offices of Microsoft Ireland.

Gilead, headquartered in the US, uses its Irish operations for the manufacture, packaging and distribution of the company's products and the supply of anti-HIV medications to developing countries. Major products for the company include Atripla (efavirenz, emtricitabine, tenofovir), the only once-daily single tablet regimen for HIV-1 infection, Truvada (emtricitabine and tenofovir disoproxil fumarate) and Viread (emtricitabine and tenofovir disoproxil fumarate) - all for the treatment of HIV infections. The company generated total revenues of \$3.03bn (€2.26bn) in 2006.

The firm will be in good company on the spot it has chosen for its new facility, the Grange Castle Business Park having specifically been designed to attract biotech and biopharma firms following an €80m investment by South Dublin County Council, and fast becoming a biotech hub for the region. The park is already home to other major pharmaceutical firms, including Wyeth who has established one of the world's largest integrated biotechnology campuses on the site at a cost of €1.8bn, used for the manufacture of biopharmaceuticals, pharmaceuticals and vaccines. Japanese firm Takeda has also invested €80m in facilities at the same site.

Gilead's further investment in its Irish operations is good news for the region, which has been suffering a little instability of late as the mixed fortunes of pharma firms in the area have caused some companies to cut down their operations while other boost their Irish investments. Despite Ireland offering one of the lowest corporate tax rates in Europe, the increasing pressure from patent expiries along with challenges from generic products and pricing competition from cheaper global locations such as Asia, have forced some pharmaceutical firms to consolidate their operations leading to job cuts and plant closures.

However, the news hasn't been all bleak for Ireland, with several major pharmas increasing their investment in their Irish operations. Only last month, for example, there were reports of a €250m investment by GlaxoSmithKline in its Currabinny plant to enable production of the active ingredient in the company's recently approved breast cancer drug, Tykerb (lapatinib). "We are operating in a highly competitive global environment for leading biopharmaceutical investment of this kind," said Micheál Martin, Irish Minister for Enterprise, Trade and Employment, on news of Gilead's plans. "A key element of IDA [Industrial Development Agency] Ireland's strategy is a focus on winning new inward investment where the activities are at the high quality end of the business value chain. Gilead Sciences will make a superb addition to the leading global biopharmaceutical companies already located [at Grange Castle]."

PharmaChemical Ireland, a group representing the pharmaceutical and chemicals industry in Ireland, valued pharmaceutical and chemical exports at over €40bn last year, with the sector having invested over €12bn in capital since arriving in Ireland in the late 1960s. Nine out of the ten top pharmaceutical companies in the world have operations in Ireland, according to the group.

## **"Drug makers shell out \$155m to sway legislation"**

**Date:** 10 April 2007

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

**Author(s):** Anna Lewcock

<http://in-pharmatechnologist.com/news/ng.asp?id=75625>

A report out this month has revealed that drug manufacturers and their trade groups spent \$155m on lobbying activities to influence US legislation in the 18 months up to June 2006. Between them, the firms and trade groups spent millions of dollars and employed the services of more than 2,000 lobbyists over the last two years to push a variety of issues for their cause.

The trade group Pharmaceutical Research and Manufacturers of America (PhRMA) was the party responsible for the biggest lobbying contribution spending \$18m last year, more than any single drug company. Since 1998 the organization has spent \$104m on lobbying activities according to the Center for Public Integrity, who published the report. Alongside PhRMA, the Biotechnology Industry Organization (BIO) is another group responsible for funding the drug industry's federal lobbying activities, though its figure is dwarfed by PhRMA's coming in at only \$34.9m since 1998. These two trade groups, combined with the contributions of the 20 largest pharmaceutical companies, funded 80 per cent of pharma firms' lobbying activities over the past nine years.

Among drug manufacturers, Pfizer shelled out the largest sum last year, spending \$12m on lobbying activities and bringing its total since 1998 to over \$62m. Merck was another big contributor, paying out around \$48m over the past nine years, with Eli Lilly, Bristol-Myers Squibb and GlaxoSmithKline not far behind, each hitting near the \$40m mark.

A spokesperson for Eli Lilly defended the company's position, saying the firm's lobbying efforts are intended to benefit the end-users of the drugs it produces: "Lilly believes it is important to the patients we serve and our business to be actively engaged in the political process," the spokesperson told US-PharmaTechnologist.com. "Over the past several years, there has been significant legislation presented nationwide at the state level that could have seriously damaged patients' access to necessary medications and the pharmaceutical industry's ability to continue its current level of innovative research." None of the other above mentioned pharmaceutical manufacturers were available to comment prior to going to press.

According to the report, one particular piece of legislation garnered much attention from drug industry lobbyists over the last year, and resulted in a bar on federal government negotiating prices of drugs supplied through the nation's Medicare system (whereas other bulk purchasers are often able to negotiate discounts with drug companies.)

Another issue that raised the hackles of the pharma industry and prompted much lobbying activity, was the possibility of allowing drugs to be imported from foreign countries and sold within the US at a cheaper price. Measures supporting such a move to allow drug imports have repeatedly been introduced in the House and the Senate, but none have successfully made it through thanks at least in part to lobbying efforts from industry.

Other matters that the pharma industry lobbied heavily included reform of the US Food and Drug Administration (FDA) to strengthen the agency's monitoring abilities - according to the report, "the industry is opposed to any legislation that would give the FDA more oversight."

Project Bioshield, a law introduced in 2004 with the aim of investing billions of dollars to stockpile vaccines and medications to protect against bioterrorism, also piqued the pharma industry's interest, apparently prompting firms to ask for added bonuses in the form of extended patent rights among other perks.

From 1998 through to June last year, drug manufacturers and their trade groups spent \$733m on lobbying activities, according to the report. The top twenty drug companies combined with PhRMA and BIO contributions totalled \$605m over the study period, with at least another \$50m being spent during the second half of 2006.

The report is part of an ongoing project by the Center for Public Integrity called 'Pushing Prescriptions', that aims to investigate the political influence of the pharmaceutical industry and its consequences on the American public.

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## 6. ANNOUNCEMENTS

### Africa Centre for Health and Population Studies: Assistant Project Leader

The Africa Centre has an exciting opportunity for an Assistant Project Leader (Ref. AC06/2007) for the **Microbicides** Development Programme (MDP) Phase III Clinical Trial. The MDP co-ordinates an international, multi-centre, randomised, double-blind, placebo controlled, phase III clinical trial to assess the safety and efficacy of PRO2000/5 **microbicide** gel in the prevention of vaginally-acquired HIV. **Microbicide** research is at the cutting edge of HIV prevention research internationally.

The Assistant Project Leader will be responsible for ensuring the effective management of the clinical trial by co-ordinating all trial activity. This post is suitable for a researcher who is interested in developing his/her project management skills or an experienced clinical research associate.

The qualifications and experience required for the post are:

- Masters degree in relevant field OR significant clinical trial management experience
- Analytical skills
- STATA experience as advantage
- Fluency in English essential
- Fluency in isiZulu an advantage
- Knowledge of Good Clinical Practice (GCP)
- Valid driver's licence
- Excellent communication and interpersonal skills
- Ability to multi-task, prioritise work loads, problem-solve, work independently and be exceptionally well organised
- Ability to initiate creative projects.

This is an exciting opportunity with a diverse workload, managerial responsibilities and the potential for scientific development. For discussions about the post, please contact Mitzy Gafos (Project Leader) on +27 (0) 72 798 3158 or Hlengiwe Ndlovu (Clinic Co-ordinator) on +27 (0) 72 268 2875.

The post will be offered on contract to March 2009, with the potential to extend at the end of this period. A remuneration package will be determined in accordance with qualifications and experience of the successful candidate.

Applicants are requested to submit a Curriculum Vitae (including three referees) and an application letter demonstrating the minimum criteria for the post, to: The Human Resources Officer, Africa Centre, PO Box 198, Mtubatuba 3935 or fax: +27 (0)35 550-7565, or e-mail: [acemployment@africacentre.ac.za](mailto:acemployment@africacentre.ac.za) quoting the relevant reference number. The process of selection will commence on 2 April 2007 and will cease only after the vacancy has been filled.

The Africa Centre for Health and Population Studies is a joint initiative of the University of KwaZulu-Natal and the South African Medical Research Council, with support from the Wellcome Trust and other funders, to create a global centre of research excellence in a rural area. The Centre's mission is to conduct in partnership with the community, policy-relevant health and population research in an ethical manner and to enhance the capacity of the people of sub-Saharan Africa to conduct research.

### **AMAG welcomes new Steering Committee members**

<http://www.global-campaign.org/amag.htm>

AMAG has invited 3 colleagues to join their Steering Committee for the year. All three individuals - Dr Elizabeth Bukusi (KEMRI, Kenya), Dr Chidi Nweneka (MRC, Gambia) and Dr Morenike Ukpong (NHVMAG, Nigeria) - have been active and supportive members of AMAG, have provided input to AMAG at many junctures, are active advocates in their own countries, and were involved in previous consultations including the AMAG planning workshop in 2005. The AMAG Steering Committee is now made up of Bernice Heloo, Chidi Nweneka, Elizabeth Bukusi, Kim Dickson, Manju Chatani (coordinator), Miriam Katende, Morenike Ukpong and Susan Thevar. For more information about AMAG, visit <http://www.global-campaign.org/amag.htm>

### **New policy documents from Irish Aid**

On March 28, Irish Aid issued a new health policy, entitled "Improving health to reduce poverty." The policy identifies five objectives for Irish Aid: (1) to address the determinants of ill health; (2) to strengthen health systems to serve the poor more effectively; (3) to promote health strategies that meet the needs of the poor and marginalized; (4) to contribute to an effective international response to health needs of the poor; and (5) to ensure a coherent approach to health improvement in all Irish Aid's work. The policy is available at [www.irishaid.gov.ie/Uploads/Health%20Policy.pdf](http://www.irishaid.gov.ie/Uploads/Health%20Policy.pdf), and a summary document is available at [www.irishaid.gov.ie/Uploads/leaflet%203.pdf](http://www.irishaid.gov.ie/Uploads/leaflet%203.pdf).

On March 27, Irish Aid announced a new five-year strategy for support of global health partnerships. The goal of the strategy is to make an effective contribution to global health initiatives and partnerships, complementary to Irish Aid support for health and HIV through bilateral and multilateral programmes. The strategy identifies four objectives: (1) to support global health partnerships for the timely delivery of effective interventions that tackle the major diseases of

poverty; (2) to maximize Irish Aid's policy influence at the global level to ensure optimal global health partnerships performance and coordination; (3) to promote best practice in country-level performance of global health partnerships, in line with Irish Aid principles; and (4) to ensure coherence between Irish Aid's support to global health partnerships and the different modalities of Irish Aid's support to countries. The strategy is available at [www.irishaid.gov.ie/Uploads/Irish%20Aid%20GHP%20Strategy\\_webversion.doc](http://www.irishaid.gov.ie/Uploads/Irish%20Aid%20GHP%20Strategy_webversion.doc).

## **New website: Resist-HIV.info**

### [Resist-HIV.info](http://Resist-HIV.info)

Resist-HIV.info is a new web-based portal sponsored by Virco Lab, Inc. It is dedicated to delivering information about drug resistance and resistance testing to all those interested in HIV resistance. Information will be provided in the form of brief clinical updates, independent expert reviews from major meetings and journals, and education programs designed to enhance knowledge about HIV drug resistance. Also included on this site is information about where to obtain HIV resistance tests, Medicare and Medicaid reimbursement codes, and links to other sources of information about HIV resistance.

## **Research Advocacy for HIV Prevention: Skills and Challenges for AIDS Activists**

During the recent Conference on Retroviruses and Opportunistic Infections (CROI) held in February in Los Angeles, CA, the Community HIV/AIDS Mobilization Project (CHAMP) and the AIDS Vaccine Advocacy Coalition (AVAC) worked with a number of partner organizations to convene "Research Advocacy for HIV Prevention: Skills and Challenges for AIDS Activists". The one-day training workshop and half-day advocacy strategy session brought together nearly 100 community advocates and activists from across the US, Europe and Asia to share information and perspectives on HIV prevention research. The report from the workshop and strategy session, as well as all of the presentations, are now available online at <http://www.champnetwork.org/index.php?name=research>

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