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TAG
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tagline

NEWS ON THE FIGHT FOR BETTER TREATMENT, A VACCINE, AND A CURE FOR AIDS

The Past, Present, and Future of HIV Microbicide Research Advocacy

AN INTERVIEW WITH POLLY HARRISON,
FOUNDER OF THE ALLIANCE FOR MICROBICIDE DEVELOPMENT

Polly Harrison founded and led the Alliance for Microbicide Development (http://www.microbicide.org) from 1998 to early 2010. She is now a senior policy advisor at AVAC. TAG worked closely with Polly in support of microbicide research and in fall 2010 TAGline interviewed her to seek her wisdom and vision for the future

TAGline: What were things like when you founded AMD?

Polly Harrison: Fairly bleak, which was why the Alliance was founded in the first place. The idea came from Mahmoud Fathalla at the Rockefeller Foundation, who provided a seed grant to form a coalition of scientists, biopharmaceutical companies, and advocates to be a "catalyst" at a time when progress toward microbicides was slow, fragmented, and woefully underfunded. There were just 20 of us at the first Alliance meeting in March 1998 but in a year we had almost 100 active participants, a database and regular reporting activities, and busy with constituency building, outreach, media work, and funding analysis. We had two staff and little money, but there was such engagement and enthusiasm that we got tons done in those early years and began to attract more funding. It's been said the Alliance "made the microbicide field" and there's truth there. People were attracted by the fact that the Alliance was a neutral convener, educator, and problem-solver. The neutrality aspect caused us problems later but it's what many value and recall, rather wistfully since the Alliance no longer exists.

You asked when the "HIV microbicide" idea was first suggested. As early as 1987, the National Institute of Child Health and Development was supporting work on "contraceptive microbicides." Then in 1990 came a hugely influential article by South African epidemiologist Zena Stein that called for "HIV prevention methods that women could use."[1] Zena argued that absent male concurrence with condom use, women had no way of protecting themselves from HIV infection, and that AIDS was becoming a women's as well as a man's disease, not a popular concept at the time.

The Alliance didn't arise in a total wasteland. Microbicides were in the

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The First New Tuberculosis Drug in Decades: Promise and Challenges

BY CLAIRE WINGFIELD

After nearly 50 years, there is finally something to get excited about in tuberculosis (TB) drug development. Tibotec's TMC207—the first compound from a novel class of TB drugs, the diarylquinolines—will likely be submitted to the U.S. Food and Drug Administration and the European Medicines Agency for accelerated or conditional approval sometime in 2011. Between the 1940s and 1970s in the first wave of the antibiotic revolution, TB—previously incurable—was first conquered by the discovery of curative drugs and combination therapy containing three or four drugs taken for six months to two years. Since 1963, when the last new class of drugs to treat TB—the rifamycins—was discovered, and in sharp contrast to the accelerated pace of HIV treatment discovery and development in the past

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portfolios of the NIH, Population Council, and International Working Group on Microbicides, in U.S. legislative language and the International Conference on Population and Development Plan of Action, and at the 1996 Vancouver International AIDS Conference, there was the first public announcement of U.S. funding for microbicide research. Still, no one had any real money, the broader HIV advocacy community was focused on therapy and later on vaccines, and the idea of something topical that could help with women's special risk was seen as scientifically and practically improbable.

The failure of the UNAIDS-funded COL-1492 trial announced at the 2000 International AIDS Conference in Durban [South Africa] didn't help! COL-1492 was a commercial product based on nonoxynol-9, which was the active ingredient in topical spermicides and also showed activity against sexually-transmitted infections. However, the trial found that COL-1492 not only didn't protect against HIV infection, but might increase that risk[2]. We were stunned by the results, didn't know how to handle them, and for a field just getting itself organized, they were traumatic and have had a long half-life.

TL: How have things changed since then?

PH: A lot. Getting an advocacy movement organized and ramped up was vital. Microbicides acquired a public "personality" and some understanding of what they were and might do, and we mobilized constituencies that got successive versions of a Microbicide Development Act introduced in three sessions of the U.S. Congress. None passed but all got introduced with a lot of education, publicity and new allies, and leveraged establishment of a Microbicide Branch [at the NIAID Division of AIDS, NIH] and a dedicated position for microbicides in the Office of AIDS Research. We helped establish the International Partnership for Microbicides and pushed steady increases in microbicide funding so NIH attracted more scientists, USAID raised its investment levels, and more developers advanced more concepts.

TL: What do you think are the leading questions facing microbicide research today?

PH: If you mean challenges to advancing toward a safe and effective product with reasonable likelihood of user adherence, I'd say:

- ***Funding***. But not just more money. I mean funding that follows and supports some kind of rational strategy and consensus among the donors about what makes sense.

- ***A distinctive collective voice speaking persistently for the special value of topical microbicides for the world's women.*** Those women *still* don't have the kind of protection from HIV infection that they need, which is why we set out to develop microbicides in the first place!

The final lessons for advocacy for microbicides and women's particular needs have not yet been told.

If you mean scientific questions, then I'd say we still don't have:

- ***Clear understanding of what kind of product will have enough potency for sufficient time to interrupt HIV transmission at key points in that process*** in ways that are safe for regular use.

- ***Even one validated biomarker*** that can give us more assurance of product use and effectiveness than even the best adherence measures we have now.

- ***A clear view of how any such product and ways to deliver it will best fit the lives of individuals and couples*** so they feel safer and make their own decisions about that safety.

TL: Do you think research on microbicides has enough political support? Enough research support? Enough commitment to do the research necessary to operationalize microbicides when we have evidence they work?

PH: Short answer: probably not. Let me take each of your questions individually.

Political support: We managed to develop a lot of political attention that, while we never got actual legislation passed, leveraged the supportive NIH responses I mentioned earlier. I don't think microbicides command that same level of political support now for several reasons:

- The image of a "movement" advocating explicitly for microbicides for women has become blurred. ***I still believe that women should have their own special "technological identity" because their needs are special***. Yes, PrEP [preexposure prophylaxis] and a vaccine would be good for both men and women, but the former has some big challenges and the latter is some years away.

- The economic environment affects microbicides as it does everyone everywhere. We can't complain since almost everyone is suffering, but we need to be especially careful and attentive because of it. Our "asks" have to be well considered, clear, and strategic. In that connection . . .

- The economy and the changed political orientation in the U.S. Congress will have impact on support for HIV across the board. What kind of impact? Enough political support? Who knows. Money is already the central issue and we haven't even gotten to competing health priorities and ideology!

***Research support*:** The economic environment obviously affects funders, who are overwhelmed, confused, and less well-resourced. In the case of microbicides, many donors lack the internal resources or standardized access to true peer review processes to make decisions, so that each donor is vulnerable to the pleadings of individual groups and their own inabilities to assess those.

Commitment: I wish I knew. Some donors clearly remain committed, but some are pressured by economic realities and

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multiplying demands. Others can't deal with the realities of scientific and pharmaceutical research, even though such research is well known to be erratic, inconclusive, sometimes just plain disappointing, before success is ever reached—if ever.

TL: What are the lessons learned from the unsuccessful microbicide trials?

PH: Like HIV vaccines, we know what we won't do again, and more about what we don't know. Did we move too fast into the clinic with not enough data? No and yes. In some cases, we didn't have the tools to know what we didn't know and couldn't answer without more human data. In others, we thought we knew more than we did, there was a sense of urgency—that, frankly, has not gone away—and we should have asked more questions sooner. As for the scientific questions, there's been much probing of those lessons by independent researchers and analysts. What we haven't done is pull those lessons together into a coherent statement to the scientific world. We do know that we won't invest in microbicide candidates that can't balance safety and efficacy in the lab—i.e., no more surfactants, no more polyanions.

TL: What are the lessons learned from the successful TDF 5% gel trial[3]?

PH: Many! The biggest and best is that the concept of a topically applied microbicide is feasible and merits pursuit. We learned that women will use such a product, their partners mostly don't seem to mind, and that women who use it most benefit the most. We also learned what we don't know: most importantly, how such a product will be used in "real life"; whether partners will continue to "not mind"; and what frequency of use will provide the necessary level of protection. And for me, one of the most important lessons was the finding that tenofovir was 51% effective in preventing genital herpes infections, and follow-on trials will be exploring that very important fact further.

TL: Are you satisfied by world reaction to CAPRISA-004[4]?

PH: I'm thrilled! Now we can say that topical microbicides have an accepted identity as an HIV prevention technology worth pursuing. We've had some long dark years sprinkled with disappointment, some loss of faith and, frankly, some disdain. To see the joy and hope in so many quarters is beyond gratifying. Not every quarter, which is distressing, but most.

TL: What plans are underway to validate that result?

PH: There are multiple plans and that's a problem. There are earnest efforts to coordinate and find consensus about what should happen next, but those are confounded by understandable vested interests, funding constraints; and maybe a bit of human cussedness. I feel better since the stakeholders meeting USAID convened a few weeks ago, where a deadline was laid down for producing a road map and timeline for next steps. There is progress in taking some regulatory steps and bridging trials are being designed. But there's no agreement about which trials will be needed to confirm the CAPRISA-004 results and by whom. Even the best road map will have to be accepted by all the key players—and there's the rub.

The microbicide movement was most effective when we had few financial resources but many committed hearts and minds, even when the political and socio-cultural environment was not welcoming.

TL: Where is the field going, and where does it need to go?

PH: We obviously have to finish what we started with tenofovir, including the VOICE trials and any other trials that are seen as necessary, and we have to be sure that the work on the dapivirine ring goes forward as the science indicates. To do all that will require major investment and we have to assure that ahead of time so that we don't have any damaging interruptions. At the same time, we can't forget the rest of the pipeline. There are roughly 70 candidate microbicides of various sorts in the preclinical pipeline and there has to be a strategy for weeding those out and supporting and moving plausible survivors. I want to see work proceed with combination products that hit HIV at various points in its nasty trajectory or can prevent more than one sexually-transmitted infection or combine such prevention with contraception. There isn't a pharmaceutical company on the planet that would ignore its earlier pipeline just because there were likely candidates in late-phase research, or ignore improving those candidates, and I'm worried that funding constraints will have that effect. The NIH plays the biggest role in the early science and we have to be sure that there's enough support there for that. If not, other funders are painfully few. We *all* have to worry about that.

TL: What are you, as an experienced microbicide advocate, planning to do now that the AMD has closed?

PH: I am really gratified to have been able to take on the role as senior advisor to AVAC. That has been useful to us both. I've been able to assure the appropriate transfer of the intellectual property that the Alliance developed over the years and to also serve as a symbol that the validity of the microbicide concept remains alive. I still seem to have a useful voice and as long as anyone listens to me, I probably will keep on talking. And there's plenty I want to write!

TL: Are there lessons for advocacy?

PH: Many. The most powerful one surprised me. The microbicide movement was most effective when we had few financial resources but many committed hearts and minds, even when the political and socio-cultural environment was not welcoming. Resource imbalances and trial failures have hurt that movement and we have not regrouped as a dedicated constituency. Some think the field has matured to the point where specific microbicide advocacy is no longer required. I disagree; much organized conversation

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and advocacy remain essential. The final lessons for advocacy for microbicides and women's particular needs have not yet been told but I'm uneasy. Ask me again next year.

TL: Do you have any other reflections you'd like to share?

Just one. In the earliest days, our circle of true friends beyond the microbicide community was small. TAG was very early among those true friends. That hasn't changed and we're so grateful. ●

Polly Harrison founded and served as director of the Alliance for Microbicide Development from February 1998 to January 2010. She was Senior Program Officer and Director of International Health at the Institute of Medicine, National Academy of Sciences, where she founded the Forum on HIV/AIDS Research and Forum on Emerging Infections, and led major studies on critical aspects of international health, infectious disease, reproductive health, and public-/private-sector responses to global health challenges. Prior to that, Polly spent two decades living and working in the developing world as a medical anthropologist, policy analyst, faculty member of the Development Studies Program, and Regional Social Science Advisor for USAID. She has since sustained those commitments as a Governing Councillor of the American Public Health Association, Fellow of the American Anthropological Association, Adjunct Professor at the Johns Hopkins University School for Advanced International Studies, member of the Board of the BioDesign Institute and the Scientific Advisory Group of the CONRAD Program, and ad hoc membership on numerous advisory panels for the National Institutes of Health. Her undergraduate and graduate degrees are from Mount Holyoke College and the Catholic University of America, respectively.

Polly's commitment to microbicides came from years of commitment to the belief that all women, those she got to know living in the developing world, her friends, and her daughters and granddaughters, have an inalienable right to those benefits of science that can make them powerful, knowledgeable, and safe.In 1998 Polly Harrison founded the Alliance for Microbicide Development (AMD; http://www.microbicide.org).

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New TB Drug in Decades, continued from page 1

quarter century, research on new TB drugs virtually ground to a halt for nearly 40 years.

It is estimated that up to one-third of the world's population—over two billion people—are infected with TB, and each one of them is a potential future case of TB disease. According to the *WHO Global Tuberculosis Control Report 2010*, TB remains the leading killer of people with HIV, accounting for at least a quarter of all HIV deaths in 2009. Despite being curable, TB claimed 4,700 lives each day—or the lives of 1.7 million people that same year.

Combination therapy for drug-susceptible TB can cure about 95% of all cases. Unfortunately, treatment for multidrug-resistant TB (MDR-TB)—a form of TB disease that has developed resistance to the two most common and powerful TB drugs, isoniazid and rifampicin—cures only 50–70% of cases and requires 18–24 months of complicated, expensive, and often toxic combination therapy. This complex treatment regimen may include up to six different pills multiple times per day plus a painful injection that can cause a long list of side effects, not the least of which may include psychosis. Most drugs used in treating drug-resistant TB are not licensed for TB treatment, and therefore their recommended use is based on anecdotal experience rather than on a body of systematically collected evidence.

But there is hope. The TB treatment pipeline is the fullest it has been in decades, with six new drug compounds—four of which are from novel classes of drugs—being evaluated in clinical trials. Tibotec Pharmaceuticals' diarylquinoline TMC207 and Otsuka Pharmaceuticals' nitroimidazole OPC-67683 are in phase IIb clinical studies for treatment of drug-resistant TB. The Global Alliance for TB Drug Development (aka the TB Alliance) has initiated phase II studies of PA824—also a nitroimidazole. Sequella's SQ-109, which is a diamine, and Pfizer's PNU-100480 and AstraZeneca's AZ5847, both oxazolidinones, round out the list of drugs in human trials.

It is expected that Tibotec Pharmaceuticals, a subsidiary of Johnson & Johnson, will seek accelerated approval for TMC207 based on the results of its phase IIb trial and initiate an expanded access program—a first for TB treatment—in mid- to late 2011. At the 41st Union World Conference on Lung Health held in November 2010 in Berlin, Tibotec's Dr. Dave McNeeley presented final data from stage 1 of the phase IIb study showing that the addition of TMC207 to a standard background regimen resulted in faster time to culture conversion and higher conversion rate—both indicators of drug efficacy—than the control arm. Study volunteers with confirmed drug-resistant TB were given standard background therapy (later individualized based on drug susceptibility testing) with those in the experimental arm also receiving TMC207 for the first 8 weeks of treatment. The median time to convert from culture positive to culture negative in the TMC207 arm was 12 weeks, as compared to 18 weeks in the control arm. The shorter time to culture conversion has significant public health implications because conversion to culture negative indicates that a TB patient is no longer infectious and able to transmit the disease. Additionally, 79% of volunteers receiving TMC207 converted to culture negative

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New TB Drug in Decades, continued from page 4

at 24 weeks versus just 58% in the control arm. These early data demonstrate the potential impact that TMC207 may have on improving cure rates and decreasing the risk of transmission of drug-resistant TB in households and the community.

A second stage of this phase IIb study comparing 24 weeks of standard background regimen plus TMC207 versus standard background regimen plus placebo has completed dosing, and follow-up is ongoing. If data from stage 2 confirm the stage 1 results that TMC207 significantly improves cure rates for people with drug-resistant TB, Tibotec will most likely pursue accelerated approval for the compound while it conducts a phase III study. The company is planning to provide the drug through an expanded access program to those with a desperate need for treatment options who cannot participate in the phase III clinical trials. While there is a precedent for expanded access to experimental drugs for use in heavily pretreated or multidrug-resistant individuals in other diseases, the dispersed nature of the MDR-TB epidemic, the scarcity of well-functioning MDR-TB diagnostic and treatment programs, and the difficult, lengthy, and toxic nature of current treatment for the disease will likely pose challenges not encountered before.

The excitement about TMC207 is tempered by the concern that despite the drug's promise, the pathway for worldwide regulatory approval is likely to be challenging. Depending on how quickly countries adapt their regulatory, diagnostic, and MDR-TB treatment programs, TMC207 may take years to roll out and become widely available to those living in high-burden, resource-limited settings. No TB drug has ever been made available through an expanded access program, making TMC207 a test case for how to ensure that a promising drug is made available as quickly as possible to those with limited or no treatment while making sure that it is used appropriately. There are lessons to be learned from HIV drug development about providing experimental drugs through expanded access. But TB poses different challenges because pharmaceutical companies believe the target market to be small and poor. In most countries TB is treated with a public health approach that prioritizes the public good over individual patient needs. In the 1990s, during the highly active antiretroviral therapy (HAART) revolution, pharmaceutical companies took on the responsibility of providing expanded access to patients in need because it helped to generate pre-regulatory demand for the drug and taught health care providers—many of them private—how to use the drug.

Because TB is a disease of the poor, many believe that there is limited potential for pharmaceutical companies to make substantial profits and that therefore they are less willing to bear the full cost and responsibility for expanded access programs—let alone the full costs of scaling up high-quality MDR-TB diagnosis, treatment, and supportive care.

The TB treatment pipeline is the fullest it has been in decades, with six new drug compounds—four of which are from novel classes of drugs—being evaluated in clinical trials.

There is also concern that if TMC207 is used inappropriately—with too few effective background drugs—new TB-resistant strains could rapidly emerge, thus limiting the drug's long-term impact on the TB pandemic.

Acknowledging these programmatic challenges and the urgent need and moral imperative to ensure access to promising TB drugs to people who are dying, TAG and others have been grappling with questions of how best to target the expanded access program for TMC207 in order to reach the individuals in greatest clinical need and to ensure that they receive care in high-quality programs without imposing unnecessary restrictions that would limit access. At the same time steps must be taken to ensure that the drug is given with appropriate active background TB therapy in the context of regular diagnostic and drug susceptibility testing to limit and monitor the emergence of drug resistance. TMC207 is farthest along in its development, so all eyes have been on Tibotec–it is encouraging that the company has taken the initiative to develop a plan for providing preapproval access to the compound. While in Berlin for the World Lung Conference, TAG met with Tibotec to review the company's draft plan for an expanded access program and provided feedback on how to broaden its scope and make it easier for well-functioning programs to provide the compound to their patients.

Poor cure rates for drug-resistant TB and the limited understanding of how best to use current drugs make the need to establish an expanded access program for new treatments for drug-resistant TB more acute than for drug-susceptible TB, and developers of these new drugs need to be prepared. Otsuka's OPC-67683 is not far behind TMC207 in its development, thus Otsuka also needs to start planning for how it will roll out an expanded access program. TAG is working with researchers, providers, and activists to develop guidance on the type of mechanism that should be in place until the drugs are available to the general public; a document is expected to be completed in early 2011 and will include what worked in providing expanded access to antiretroviral drugs but will focus on addressing the specific challenges facing TB patients, health care providers, and national TB programs in accessing experimental treatments.

There are only a few persons left working in TB who can remember the discovery of the last class of drugs, so after many years of so little, the promise of TMC207 and the current activity in TB treatment research has generated an uncommon feeling of excitement in the field. The ability to drastically improve treatment outcomes for people with drug-resistant TB and make treatment for drug-susceptible disease easier to complete finally feels within reach. ●

HIV/AIDS Clinical Trials Network to Take On New Research Priorities Under Severe Funding Constraints

BY COCO JERVIS

Big changes are planned for the $300 million AIDS clinical trials networks funded by the U.S. National Institutes of Health (NIH). Founded in 1987 at the height of the AIDS crisis, the networks are credited with numerous groundbreaking clinical advances in HIV and opportunistic infection prophylaxis and treatment that has prevented countless infections and saved millions of lives. From opportunistic infection prophylaxis and combination antiretroviral (ARV) therapy, to prevention of mother-to-child transmission, to preexposure prophylaxis and antiretroviral microbicides, much of our current knowledge on how to manage and prevent HIV was tested and proven effective in trials conducted by NIH-sponsored networks in domestic and international research institutions with teams of investigators and—most important—the cooperation of tens of thousands of study volunteers. Given the centrality of these networks to AIDS research and their long history of community participation, the restructuring process is being closely watched by both researchers and AIDS activists as it will affect the research agendas and priorities for the next decade.

Accounting for approximately 10 percent of the $3 billion NIH AIDS annual budget, the networks currently have the largest portfolio of HIV/AIDS clinical research in the world. With a seven-year funding cycle set to expire at the end of 2012, the networks will be restructured to take on new and complex research challenges emerging from the evolving HIV epidemic, maintain ongoing research into vaccines and biomedical prevention, and renew emphasis on the search for a cure all the while operating under the threat of drastic U.S. congressional funding cuts in the coming years.

Emerging Research Priorities

While various treatment strategy trials such as treatment intensification and treatment interruption have not yielded favorable outcomes, the replacement of older and more toxic ARVs with newer and more tolerable drug combinations has lead to lower rates of treatment side effects and more durable, potent antiviral activity. The drug development industry has the search for novel antiretroviral compounds and classes well in hand, enabling publicly funded HIV clinical research to move away from run-of-the-mill antiretroviral drug development to focus on curing HIV, ameliorating AIDS-related aging, and focusing on pressing conditions that are killing people with HIV worldwide. These include tuberculosis (TB) and hepatitis C coinfection (HCV) and a host of comorbidities, complications and non-AIDS cancers. Recent research has established the need for investigation into the role chronic immune activation and accelerated immunosenescence play in earlier onset of aging-related conditions in people with HIV, arguing for a new multidisciplinary focus on AIDS and aging in the newly configured networks.

In order to stem HIV morbidity and mortality associated with these conditions, the networks will need to reevaluate their research priorities and bring in new leadership with expertise in these critical areas. Over the past two decades the networks' leadership has frequently been criticized for its resistance to collaborate with outside experts, making multidisciplinary research difficult. Additionally, the mentoring and training of young investigators is desperately needed to ensure robust HIV research into the future. These are all compelling reasons for the new network structures to be more flexible to encourage cross disciplinary collaborations.

While the research agenda is still a work in progress, the leadership of the National Institute of Allergy and Infectious Diseases (NIAID)—the lead NIH institute on AIDS—and its Division of AIDS (DAIDS) have highlighted key areas that they would like to focus on. The therapeutic research priorities will be on TB and HCV coinfection, and other comorbidities including those associated with HIV and aging, novel drug approaches such as weekly dosing, and working toward a cure or a functional cure, meaning viral suppression without the use of ARVs. TB and HCV will be studied both in people with and without HIV coinfection. For vaccine research, priority areas will involve phase I, II, and III vaccine strategies as well as therapeutic vaccines. In prevention research the focus will be on microbicides, preexposure prophylaxis, emerging products, and test-and-treat methods. The networks will be organized to ensure infants, children, adolescents, and pregnant women are also included in all major research activity. For pediatric research, priority areas will include pharmacology and drug formulation issues as well as prevention.

During the NIAID town hall meeting in October 2010, NIAID director Dr. Anthony S. Fauci and DAIDS head Dr. Carl Dieffenbach highlighted these coming research priorities and stated that they are seeking more transparent and collaborative mechanisms in network infrastructure and governance and are looking for innovative avenues through which to incorporate new expertise and expand community involvement. They want to create an infrastructure with multidisease research capacity so that each clinical trials unit (CTU) can be reconfigured as needed.

In terms of overall network governance there will be an overarching cross cutting strategic working group that will be open to community participation to shape the

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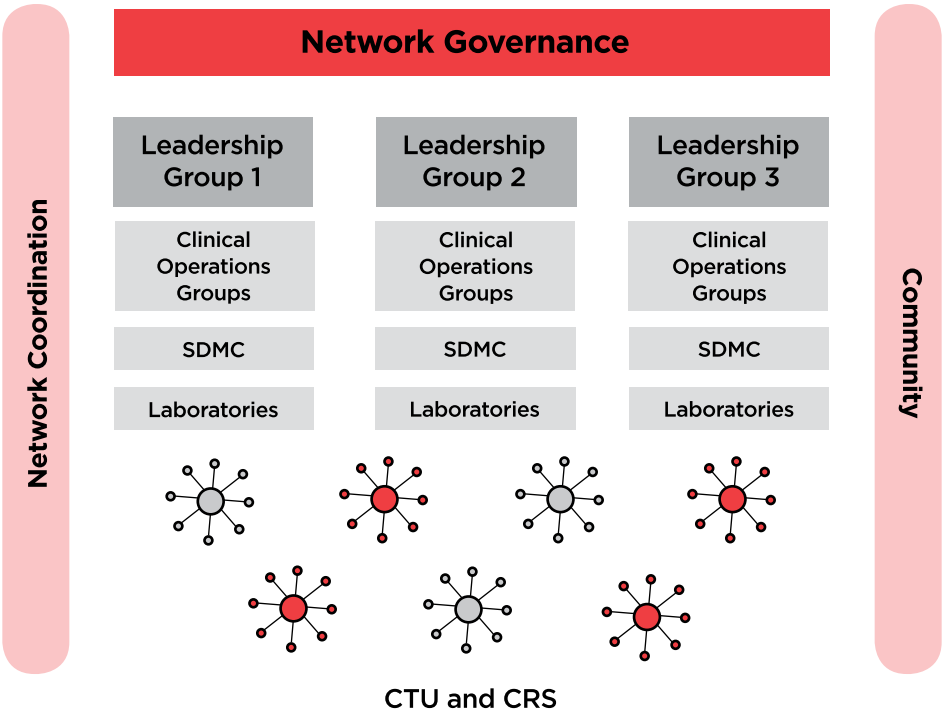
HIV/AIDS Clinical Trials Network, continued from page 6

vision of the network, review network strategic plans, and monitor clinical trials and transagency collaboration. An operations working group will be responsible for implementation issues and resource utilization.

Currently there are over 73 CTUs worldwide. This number is expected to be reduced by two-thirds with each new CTU overseeing four to eight clinical research sites. All CTUs will perform HIV/AIDS research, and some will be able to perform non-HIV research (e.g., research into HCV, TB, and aging). The future CTU reconfiguration may consist of two different types of sites. The first would include stable and protocol-specific clinical research sites that would have surge capacity; the second would be flexible sites with streamlined procedures for adding or eliminating clinical research sites. The reconfigured CTUs would have increased authority and accountability to perform capacity management, resource sharing, and utilization and cost-containment measures. Questions remain as to how the new structure will advance the capacity to perform HIV, HCV, and TB treatment trials internationally, particularly in resource-limited settings as well as in venues such as methadone clinics and correctional facilities.

Over the past year, the Treatment Action Group put forth recommendations to NIAID and the HIV community on network infrastructure and priority agenda-setting for HIV therapeutics, viral hepatitis, and TB. The comment period for the community is set to expire in February 2011. To read TAG's recommendations visit *http://www.treatmentactiongroup.org/networkrestructure.aspx*. To join in the overall network restructuring discussion with your ideas or questions visit *http://blog.aids.gov/2010/06/restructuring-niaids-hivaids-clinical-trials-networks.html*.

2013 Network Structure



Dec 2010

Source: Dr. Carl Diffenbach, DAIDS.
SDMC – Statistical and Data Management Center

Microbicide Field Wrestles with the Implications of Success—An Update

On October 25, 2010, the nonprofit microbicide research organization CONRAD announced that the U.S. Food and Drug Administration (FDA) would consider the Vaginal and Oral Interventions to Control the Epidemic (VOICE) trial as a confirmatory trial to the CAPRISA 004 results (see *TAGline* vol 17, no. 3). Further, the FDA has agreed to accept fast-track designation for the 1% tenofovir gel microbicide, meaning that the clinical trial sponsor may submit completed sections of the new drug application for review by the FDA rather than waiting until the entire application is complete. This can speed the way for approval if the VOICE trial results confirm those obtained in CAPRISA 004. The FDA did identify some specific additional information that will be required, including safety data in adolescents, in-vivo drug interaction studies with commonly used vaginal products, and data on postmenopausal women. In addition to VOICE, follow-up trials in South Africa will proceed, but the fate of a larger multicountry study planned by the UK's Microbicide Development Programme (named MDP302) remains uncertain; after the CONRAD announcement, the MDP issued a statement welcoming the FDA's decision but also explaining why they feel MDP302 is still justified.

To see the CONRAD announcement go to *http://www.conrad.org/news.html*

To see the MDP response go to: *http://www.mdp.mrc.ac.uk*

TAG NEW WAYS TO CONTRIBUTE

Supporting TAG is a wise investment in AIDS treatment advocacy. With a small but well-organized and highly respected staff of professionals, every donation to TAG brings us one step closer toward better treatments, a vaccine, and a cure for AIDS. There are several ways you can support TAG today!

Make a tax deductible gift now by credit card using our secure website (www.treatmentactiongroup.org) or by calling Joe McConnell at 212.253.7922 to request a donation envelope.

Celebrate!
Expand your support for TAG by asking your friends and family to make a donation in your honor to celebrate your birthday, anniversary, or the holidays. An acknowledgment will be sent to donors, and you will be informed of gifts made in your honor. Please call Joe McConnell at 212.253.7922 to request that materials be sent to friends and family.

Support TAG's
Research in Action Awards
Each December, TAG's Research in Action Awards event honors some of the most important scientists, artists, celebrities, and activists working for better treatments, a vaccine, and a cure for AIDS. Past honorees and presenters have included New York State Senator Tom Duane, researcher Dr. Trip Gulick, executive director of the Global Fund Michel Kazatchkine, award-winning playwright Terrence McNally, actor David Hyde-Pierce, and stage and screen actress Kathleen Turner, among many other scientists and dedicated AIDS activists. Join us this December!

Does your company have a matching gifts program?
If so, you can double or even triple the donation you make to TAG. If your company offers a matching gifts program, please complete its matching gift form and send it in with your donation to TAG.

Make a gift of stock to TAG
Gifts of stock benefit TAG and the donor. The donor who purchased the stock at a lower price receives the tax deductible benefit of the stock's price on the day it is transferred to TAG.

For more ways to support TAG, please visit our website at www.treatmentactiongroup.org or contact Joe McConnell at 212.253.7922.

TAG BE INVOLVED

About TAG

Treatment Action Group is an independent AIDS research and policy think tank fighting for better treatment, a vaccine, and a cure for AIDS. TAG works to ensure that all people with HIV receive lifesaving treatment, care, and information. We are science-based treatment activists working to expand and accelerate vital research and effective community engagement with research and policy institutions. TAG catalyzes open collective action by all affected communities, scientists, and policy makers to end AIDS.

Program areas include antiretroviral treatments, basic science, vaccines, prevention, hepatitis, and tuberculosis.

Join TAG's Board

TAG is always seeking new board members. If you are looking for a great place to invest your time and talents, please call Barbara Hughes, TAG board president, to learn more about board opportunities with TAG.

Call 212.253.7922 or email:
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