

Minding the Gaps: The Forum for Collaborative HIV Research (FCHR)

By Tim Horn with Theo Smart

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The old adage, "The more you learn, the less you know," has never been truer than when applied to the medical management of HIV disease, though it is easy to forget how far we have come in a relatively short period of time. The advent of highly active combination therapy, viral load testing, and drug-resistance testing has essentially revolutionized the field of HIV care. At the same time, fundamental questions remain—most notably when and how to use these powerful tools in the face of drug resistance, side effects, gender and racial disparities, and limited financial resources—that have yielded conflicting concerns and opinions among the various communities with a stake in HIV research: clinicians, academics, government, the pharmaceutical industry, and HIV-infected patients themselves.

It will undoubtedly take a collective effort to sort through these lingering questions—along with challenges and paradoxes that have not yet surfaced—and to determine how best to transfer evolving trends in HIV research into safe and feasible clinical practice. For this, there is the Forum for Collaborative HIV Research. As explained by Dr. Roy "Trip" Gulick, Co-Chair of the Forum's Executive Committee and Associate Professor of Medicine at the Weill Medical College of Cornell University in New York, the Forum was recently established to explore the most important research questions and to nurture scientific efforts in those areas. "As an independent group," Dr. Gulick explains, "the Forum seeks and develops consensus from the diverse constituencies represented with the singular goal of moving HIV/AIDS research forward. To date, the Forum has been very successful in identifying, evaluating, and catalyzing the next steps in the key areas of HIV research."

In this way, the Forum differs from other consensus-driven collectives, most notably treatment guideline panels spearheaded by the United States Department of Health and Human Services and the International AIDS Society-USA. The Forum goes beyond formal reviews of current research and practice patterns in an effort to clearly identify gaps in the current knowl-

edge base of HIV care and to make recommendations on how to fill them. In this way, the Forum and its published proceedings have become a crucial source of supplemental information for clinicians. Yet it is a resource that many HIV care providers have not yet fully realized.

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Veronica Miller, PhD
Executive Director, FCHR

Laying the Cornerstone

The Forum began its work on March 1, 1997—under the directorship of David Barr, JD, a longtime treatment and public policy advocate for HIV-positive people—and remains situated at the George Washington University School of Public Health and Health Services in Washington, DC. Its history actually dates back further, to February 1996, when Vice President Al Gore held a meeting with leaders from the pharmaceutical industry and other government officials to discuss further steps in drug development for HIV-positive people. The Clinton administration was less interested in the development of new compounds—after all, saquinavir (Invirase) had been approved a few months earlier, and nevirapine (Viramune), indinavir (Crixivan), and zidovudine (Retrovir) were all scheduled to be approved in 1996—but remained eager to collaborate with all major stakeholders to better understand the clinical utility and long-term effectiveness of antiretroviral therapy.

At the Vice President's request, the Keystone Center, a public-interest organization coordinating discussions on scientific and

environmental issues, held a series of meetings between representatives from the pharmaceutical industry, public and private insurance programs, government agencies, clinical research centers, and patient advocacy groups to discuss HIV medical management issues in the emerging era of HAART, research design and methodologies, and the establishment of a framework to promote collaboration.

With the conclusion of these meetings, a report was generated proposing the development of a project to continue key discussions among stakeholders regarding the study and implementation of long-term antiretroviral treatment strategies. The report was presented to the Vice President on August 2, 1996, further recommending that such work and guidance continue through the creation of The Forum for Collaborative HIV Research.

Something for Everyone

The Forum is now under the leadership of Veronica Miller, PhD, who began as Executive Director in September 2001 and is perhaps best known for her Frankfurt-based research on HIV treatment strategies, such as her studies focusing on the immunological and virological effect of structured treatment interruptions. Ben Cheng, arguably one of the brightest and most respected HIV-treatment advocates, recently joined Dr. Miller and will now be serving as Project Manager of the Forum.

With Dr. Miller and Mr. Cheng at the helm, the Forum is poised to "continue bringing the right people together within an established infrastructure to address key research opportunities in HIV/AIDS," says Diane Goodwin, Pharm.D., Dr. Gulick's Co-Chair of the Executive Committee and a faculty member of the HIV Division at GlaxoSmithKline.

Dr. Goodwin suggests that with industry representatives such as herself, along with the numerous experts from around the world who participate in the Forum's reg-



Veronica Miller, PhD
Executive Director,
Forum for Collaborative
HIV Research

ular workshops, there is now tremendous opportunity for scientific cross-pollination. "Relationships developed through Forum participation often lead to opportunities for both formal and informal collaborations to advance HIV/AIDS research and patient care," she says.

Dr. Miller concurs and believes that, as a result of current and future research collaborations being nurtured by the Forum (see Sidebar), pivotal studies being developed and performed by the various research entities can begin faster, and duplication of efforts can be reduced. Patient enrollment and retention can be enhanced, the costs of getting answers to critical questions shared, and the results of research can be put to better and more expeditious use.

Forum-inspired collaborations begin with the bringing together of experts who review the state-of-the-art for a particular topic, followed by workshop participants making recommendations regarding how to drive the field forward. "By publishing the reports we make this information available to the medical, scientific and patient community at large," Dr. Miller explains (all published reports can be downloaded from the Forum's Web site: <http://www.hivforum.org>). "In addition, we are developing a new strategy to follow up on the outcome of the workshops and meetings."

Among the new follow-up activities the


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Forum is engaging in are: debriefing sessions with the sponsoring and other appropriate agencies; following up with the planning committees and workshop participants to survey for new research initiatives that they are either engaged in or aware of that are direct outcomes of our workshop; and publishing follow-up reports on the Web site, describing achievements made in the 12 months following the conclusion of the workshop, along with a list of all new grant initiatives, new research collaborations, and other activities that take place. "In our follow-up program we will of course work with all of the constituencies—including industry representatives, research networks, and advoca-

cacy groups—and not just hit on the agencies," adds Dr. Miller.

As for HIV-treating clinicians, who have long been at the forefront of the epidemic and may not feel as if they have a voice in the identification of knowledge gaps or the formulation of research recommendations, the Forum has a great deal to offer. James Braun, DO, Founding President of Physicians' Research Network (PRN) and Editor-in-Chief of *The PRN Notebook*, was recently appointed to the Executive Committee to represent HIV-treating clinicians and will serve as an emissary to bring questions and concerns facing primary care providers to the forefront of the Forum's agenda.

"For practicing clinicians, the points of interest are the background documents that are prepared, which review the state-of-the-art for that field, as well as the summaries of the plenary talks that are presented to the workshop participants," Dr. Miller explains. "It will also be of interest for clinicians to read the recommendations that are made in the sense that it gives them an indication of where the field is going—how it is evolving. Additionally, clinicians who are aware of new and upcoming problems can use PRN and the Executive Committee representation to bring these issues to the Forum's attention." A voice for everyone, indeed. 

The Forum for Collaborative HIV Research: Current and Planned Projects

Monitoring Long-Term Toxicities of HIV Treatments

The Forum will bring together international experts in the field of pharmacoepidemiology, antiviral treatment and toxicities, and health resource utilization from academia, government agencies, the pharmaceutical industry, and the treatment and patient communities to:

- Catalog and assess the strengths and weaknesses of the existing mechanisms for capturing adverse events, identifying the gaps in the current surveillance activities;
- Develop recommendations for improvements in current surveillance systems and/or the design of new systems (e.g., signal detection);
- Discuss the requirements for a successful international, continuous and long-

term oversight of this process and make recommendations for how to set this up; and

- Develop recommendations for appropriate action to follow signal detection.

STATUS: The first workshop was held on April 17 and 18, 2002; a second workshop is planned for the fall of 2002.

Definition of Antiretroviral Treatment Failure

The Forum has convened a working group composed of international experts in the field of antiviral therapy, drug resistance, health resource policy and utilization, drug toxicity, cohort studies databases, clinical trials group databases and analytic approaches from academia, government agencies, the pharmaceutical industry, and patient communities. This group is meeting

on an ongoing basis in an effort to:

- Discuss and publish a comprehensive state-of-the-art view of treatment failure;
- Make recommendations for new approaches to data collection that will facilitate more comprehensive analyses of treatment failure and distinguish amongst the various forms of treatment failure;
- Make recommendations for new analytic approaches to assess treatment failure in a comprehensive manner; and
- Recommend specific analyses to assess the scope of treatment failure as needed for individual patient management, public health issues and drug development.

STATUS: The working group met in December 2001 and will continue to convene on an ongoing basis.

Standardization and Clinical Relevance of HIV Drug Resistance Testing

The Forum will convene a workshop with international experts in the areas of genotypic and phenotypic resistance testing, technology development and standardization, database systems and analysis, cost-effectiveness and health resource utilization from academia, government agencies, pharmaceutical industry, diagnostic industry, treatment community and patient community with the goal to:

- Identify clinical databases suitable for the generation of genotypic algorithms and phenotypic cut-offs;
- Develop analytic approaches for the derivation of virologic response-associated definitions of resistance for each anti-retroviral drug;
- Establish collaboration among the various constituencies to facilitate the performance of the required analyses;
- Review current regulatory aspects related to standardization and quality assurance including laboratory as well as genotype interpretation issues;
- Present and publish the overall findings to the relevant government drug and technology approval agencies (FDA and EMEA); and
- Make recommendations for how best to establish a continuous and long-term evaluation of clinically defined HIV drug resistance.

STATUS: The overall planning committee has been formed and met in the spring of 2002.

Gender Issues in the Management of HIV Disease Care, Prevention and Research

The Forum will convene a workshop in collaboration with the Office of AIDS Research, National Institutes of Health, and the Centers for Disease Control and Prevention, to focus on selected specific issues. The workshop will address sex and gender issues with respect to antiviral treatment, treatment associated toxicities and vaccine research. The workshop will also address how gender issues (e.g., parenthood and sexuality) affect prevention and care of HIV disease. The group of international experts will be asked to develop recommendations for innovative research agendas and changes to current agendas that will facilitate progress in this area.

STATUS: The planning committee met on May 22.

Racial and Ethnic Minority Issues in the Management of HIV Care, Prevention and Research

The Forum will convene a workshop in collaboration with the Office of AIDS Research, National Institutes of Health and the Centers for Disease Control and Prevention, to focus on actions required to close the gaps in research of racial and ethnic minority disparities with regard to recruitment and retention in clinical trials, prevention efforts, genetic factors associated with treatment response, drug disposition and toxicity, as well as vaccine research. The group of international experts will be asked to develop recommendations for innovative research agendas and changes to current agendas that will facilitate progress in this area.

STATUS: The planning committee for this project is in formation

Quality of HIV Care—Closing the Gap

In collaboration with HRSA, the Forum will convene a workshop to address the supports that can be provided to close the “quality gap” between high-volume and low/mid-volume providers. The participants of this workshop will consider what criteria describe quality care, the impact of certification for low-prevalence and other underserved areas and possible support systems for low- and mid-volume HIV medical providers.

STATUS: The planning committee for this project is in formation.

Transfer of Diagnostic and Monitoring Technologies into Resource-Poor Settings

The Forum has been asked to convene a meeting bringing together the key players of the various academic programs and networks operating in resource-poor settings (both local and international), relevant government agencies (NIH, CDC, FDA) and diagnostic industries to specifically focus on alternative assays used to measure CD4 cell count (Dynabeads, Cyto-spheres, modified flow-cytometry based assays), assays to measure plasma HIV levels (modified p24 assay), assays utilizing dried blood-spots and methods to improve sample stability for shipment. The international expert group will be asked to address the following objectives:

- Assess the current use and validation status of these assays;

- Assess the projected utilization of these assays in planned clinical research activities;
 - Identify the requirements for clinical validation and acceptance;
 - Obtain commitment from the respective participants to implement the necessary steps toward clinical validation;
 - Develop recommendations for continuation of this process for newer technologies as they are ready to enter clinical trial phases.
- The outcomes for this project include a published report of the proceedings, a technical assistance monograph(s) outlining the process of clinical validation for new technologies in international settings, and a Satellite Symposium, XIV International AIDS Conference, Barcelona 2002. Surveys and evaluation of the process will be undertaken at regular intervals to assure that clinically validated alternative technologies are in place.

STATUS: The first Forum workshop on this topic was held on April 22, 2002 (see the report on the Forum’s Web site).

Establishing Collaborative Networks Among HIV-Related Academic Programs in Africa

The Forum plans to convene a series of focused meetings of major academic HIV-associated programs operative in Africa, to discuss opportunities for collaborative and cooperative networks that would enhance the benefit brought by each of the individual programs. The workshop will be representative of the major academic programs, with balanced local and international leadership.

STATUS: The steering committee for this project is currently being developed.

1983–2003: How has HIV changed over the last 20 years and what changes can we predict for the next 20 years?

2003 marks the 20-year anniversary of the discovery of HIV. The Forum will sponsor an open mini-conference to review the molecular epidemiology of HIV clade distribution on a global scale, changes in HIV from immune selection and changes in HIV from drug selection. What changes can we expect over the next decades? How will that affect the course of disease? Will we be prepared to treat the 2023 version of HIV?

STATUS: The steering committee for this mini-conference is currently being formed.