

***2nd Global Experts Summit:
Leading by Example in the
Public Health Approach to ART***

**Fairmont Hotel Vancouver
900 West Georgia Street
Vancouver, Canada**

11 – 13 February 2009



Message from the President of the International AIDS Society

Dear Colleague:

I am writing to share details with you of the IAS-convened global experts' summit "Leading By Example in the Public Health Approach to Antiretroviral Therapy." The meeting will take place in Vancouver, Canada from February 11-13, 2009.

As a signatory to the WHO Consensus Statement on August 4, 2008, the IAS confirmed its support along with the Global Fund to Fight AIDS, Tuberculosis and Malaria and the World Bank for the effective and efficient implementation of the public health approach to ART in low and middle-income countries (LMIC). As part of that work, we outlined four policy-relevant priority research areas aimed to sustain and improve this approach in low and middle-income countries.

The Vancouver summit will focus on the first of these priority areas: research gaps in antiretroviral therapy. We already know that ART saves and extends lives. Our goal in this critical dialogue will be to identify major knowledge gaps, and obstacles to optimizing the individual and societal benefits of ART, as well as the strategies needed to address these.

Over the course of two-days, we will explore innovative research questions and tackle major challenges surrounding initiation, optimization and delivery of ART in low- and middle-income countries (LMIC): When should ART be initiated? What is the optimal time for switching to second-line and salvage regimens, and what combinations and formulations should be used? What is the impact of HAART on HIV prevention?

Your participation in the summit will help us translate ART knowledge into evidence-based action. Not only is your support key to the success of the event, but also to the overarching goal of Universal Access to ART by 2010.

I look forward to your participation.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'Julio Montaner', written in a cursive style.

Dr. Julio Montaner

Co-Organizers

- The Global Fund to Fight AIDS, TB and Malaria
- The World Bank

Co-Hosts

- BC Centre for Excellence in HIV/AIDS
- Public Health Agency of Canada

Industry Sponsors

- Abbott
- Boehringer-Ingelheim
- Bristol-Myers Squibb Foundation
- Gilead
- GlaxoSmithKline
- Merck
- Schering-Plough
- Tibotec

I. The Global Reality of Antiretroviral Therapy

The heaviest burden of the epidemic continues to fall on low and middle-income countries (LMIC). To overcome such challenges and meet the collective commitment to Universal Access to Treatment by 2010, the international community has embraced the *public health approach* to deliver antiretroviral therapy and care. This approach has been widely endorsed as the most effective way to scale up and deliver HIV treatment and care, particularly, but not exclusively, in resource-limited settings.

Despite ongoing international efforts to narrow the divide between the North and South, large gaps still exist in access, knowledge and resources surrounding the treatment and care of people living with HIV/AIDS. In fact only 3 million of the more than 7 million people in urgent need of antiretroviral therapy (based on current WHO treatment guidelines) in LMIC are actually receiving treatment (Towards Universal Access: Scaling up priority HIV/AIDS interventions in the health sector, WHO/UNAIDS/UNICEF, 2008).

The international community has mobilized efforts to keep up with the demand for ART. Still, the rapid rollout of HIV treatment programmes has presented large and unique challenges. For instance, many countries do not have the health care or laboratory infrastructure to implement and monitor ART based on existing guidance, a problem that will be compounded as more and more persons in need are placed on treatment. These challenges will be compounded as increasing numbers of people require second line and salvage ART regimens. Research and resources are needed to anticipate and address these issues.

In the face of rapidly growing resource demands for ART and the strain on health care systems, prevention has become even more urgent. Recent modeling suggests that universal testing and treatment regardless of CD4 count or disease stage could have a dramatic impact on HIV transmission (Granich, R et al. Universal HIV Testing with Immediate Antiretroviral Therapy as a Strategy for Eliminating HIV Transmission, *Lancet*, 26 November 2008). How such a strategy would be implemented - which in the short term would require substantially more resources, although ultimately deliver costs savings - represents yet another challenge to the HIV field.

Based on the outcomes of key meetings to date, the prioritization and implementation of operations research is ultimately a top concern: “[R]esearch ...is vital to implementing the public health approach more effectively and to establishing the evidence base required to strengthen and expand HIV treatment and care scale-up in the developing world,” (WHO Consensus Statement, August 4, 2008).

II. Vancouver Summit on ART: Moving Knowledge into Action

From the evening of 11th through 13th February 2009, immediately following the Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal, experts will gather in Vancouver, Canada to update research priorities and agree on a plan for addressing the knowledge gaps in the public health approach to delivering antiretroviral therapy and care in low and middle-income countries.

Dr. Julio Montaner, IAS President and Director of the BC Centre for Excellence in HIV/AIDS, will host the two-day summit, which is aimed at promoting quality, evidence-based decision-making through a series of innovative scientific presentations, review of the most recent data, and sharing of existing best practices. The summit will also foster multilateral collaboration in the scale up of ART using the public health approach.

SUMMIT GOAL

- To develop expert consensus on research needed to optimize the individual and societal benefits of the public health approach to delivering ART

SUMMIT OBJECTIVES

- To evaluate and build consensus on the most recent scientific data on ART with a focus on initiation, optimization, monitoring and delivery;
- To identify additional research required to identify how to maximize the preventive benefit of ART
- To identify key actions by each partner to strengthen human and financial investment in capacity-building and implementation of a robust operations research agenda

III. A Timely Opportunity

For several years now, the international community has advocated and increasingly implemented a public health approach to ART in LMIC. Where specialized physicians and advanced laboratory testing are not practical realities, the public health approach, based on simplified, standardized treatment strategies and decentralized delivery of services, has made it possible to extend the benefit of ART to millions of HIV infected individuals in desperate need.

An examination of expert meetings and conferences from the past year presents a clear evolution of advocacy, knowledge-exchange and collaboration around the public health approach to ART. And the coming year is ripe with opportunity to continue in the same stead. From small working group meetings to a new Operations Research Track at IAS 2009, the international community is working to continually refine this strategy for treatment and care.

“As a signatory to the WHO Consensus Statement on August 4, 2008, the IAS confirmed its support for the effective and efficient implementation of the public health approach to ART in LMIC.”

Still, there are many questions to be answered, knowledge gaps to fill, research to mobilize and resources to secure. By building on important lessons from the recent past and using them to advocate for and shape the future, the Vancouver summit and its participants will be well poised to help further optimize the individual and societal benefits of ART.

Building on the Past:

- **WHO Working Group Meeting**
Prioritizing Second-Line Antiretroviral Drugs for Adults and Adolescents: a Public Health Approach, Geneva, May 2007.

Participants developed consensus on the selection and prioritization of second line ARVs and recommended that they be made available to national programmes. The meeting report is available at:

http://www.who.int/hiv/pub/meetingreports/art_meeting/en/index.html)

- **IAS Sydney Declaration**
Good Research Drives Good Policy and Programming, Sydney, July 2007 (at the 4th IAS Conference on Pathogenesis, Treatment and Prevention).

The declaration was developed in advance of the conference as a call for the scale up of research, particularly operations research, in the context of ART rollout. It is premised on the understanding that the response to HIV/AIDS requires a sustained commitment to ensure that interventions and approaches to service delivery are continuously improved over time. “[Signatories are calling] on national governments and bilateral, multilateral, and private donors to allocate ten per cent of all resources dedicated to HIV programming for research towards optimizing interventions utilized and health outcomes achieved.” The Declaration was featured in the July 7, 2007 edition of *The Lancet*. Individuals and organizations are still invited to sign-on support through the IAS website at <http://www.iasociety.org/Default.aspx?pageId=63>.

- **WHO Consultation**

Addressing knowledge gaps in the public health approach to delivering antiretroviral therapy and care, Geneva, March 2008.

Co-sponsored by the IAS, the World Bank and the Global Fund, this experts meeting brought together leading clinicians, community advocates, programme managers, researchers, donors and normative agency representatives. The group produced a Consensus Statement, which underscores research as vital to implementing the public health approach effectively and efficiently. In the statement, the partners agreed to advocate for the funding and implementation of research required to implement the public health approach more effectively and to establish the necessary evidence base to strengthen and expand HIV treatment and care scale-up in LIMCs. The co-sponsors also agreed to advocate for the funding and implementation of the research activities identified at the consultation; to build collaborations with countries to encourage greater investment in policy-relevant research; to work closely with partner agencies and low and middle-income countries to build capacity for evidence-based practice; and to contribute organizational resources to see these commitments through. Implementation issues related to addressing research gaps were discussed but not featured, and the Vancouver summit provides an opportunity to extend the conclusions of the WHO Consultation. http://www.iasociety.org/Web/WebContent/File/consensus_A4_web_en.pdf

- **XVII International AIDS Conference**

“Universal Access Now”, Mexico City, August 2008.

AIDS 2008 will be known as the conference where ‘treatment married prevention.’ In keeping with their commitments from the WHO Consensus Statement, key agencies co-sponsored a session to achieve wider agreement on an implementation strategy for the key actions outlined in the consensus document. The concept of treatment as prevention received particular attention.

Shaping the future:

- **Conference on Retroviruses and Opportunistic Infections (CROI)**

Montreal, February 2009

CROI brings together many of the world’s leading HIV/AIDS researchers in a scientifically focused meeting working to understand, prevent, and treat HIV/AIDS and its complications. This will provide both momentum and fresh scientific information for the proposed summit.

- **5th IAS Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2009)**

Cape Town, July 2009

Operations research will be a central focus of IAS 2009 through the new Operations Research Track. The track will focus on applied research and other analyses designed to improve the quality and implementation of HIV programmes and policy. Key outcomes of the Vancouver Summit can be used to frame discussions in Cape Town and advance scientific agendas. A special lunchtime session at Cape Town will be devoted to reporting back on the discussions and decision-making at the Vancouver Summit.

- **IAS Industry Liaison Forum (ILF)**

Cape Town, July 2009

The ILF's mission is to remove barriers to research investment by the pharmaceutical industry in resource-limited settings. By including industry in the Vancouver Summit, key outcomes of the meeting can be linked to the ILF's agenda with potential for advancing the public health approach to ART.

IV: One Critical Focus: Policy-Relevant Research and ART

The WHO Consensus Statement identified priority-relevant research within four broad categories. In order to thoroughly probe, evaluate, and critically assess the issue, the summit will focus entirely on the first theme: research gaps within the area of antiretroviral therapy. Over the course of two-days, participants will explore innovative research questions and tackle major challenges surrounding the initiation, optimization and delivery of ART in resource-poor settings.

“Our goal in this critical dialogue will be to hone in on the major gaps in knowledge, as well as other obstacles to optimizing the individual and societal benefits of ART.”

The report from the WHO Consultation in March 2008 provides invaluable insights into the research gaps surrounding ART. Issues raised and research and experiences shared will be integral to discussions in Vancouver. A summary of major ART issues as identified and articulated in the WHO document are reflected below and cited here (Addressing Knowledge Gaps in the Public Health Approach to Delivering Antiretroviral Treatment and Care: Research for Action: Report from a Consultation).

Prevention:

- **What is the impact of HAART on HIV prevention and how can it be enhanced?**

Despite substantial efforts in terms of prevention, education and harm reduction, HIV continues to spread. A successful preventive vaccine is at least many years away. New prevention strategies, including circumcision, have shown promise but remain substantially underused. Microbicides, vaccines and immunotherapies remain potentially attractive despite recent disappointing research results. In contrast, antiretroviral drugs have proven to be highly effective in the mother to child transmission setting. The role of antiretroviral therapy in the prevention of HIV transmission in other settings has been increasingly discussed in the literature and at international conferences. In brief, in countries where ART is widely available,

research demonstrates that its use has dramatically decreased AIDS morbidity and mortality and transformed HIV/AIDS into a chronic and manageable illness. Population studies in Taiwan and Vancouver have shown that the expansion of ARV therapy programs between 1996 and 1999 was associated with an approximately 50% decrease in new HIV infections that could not be accounted for by decrease in risky behaviours (Fang CT et al. Decreased HIV transmission after a policy of providing free access to highly active antiretroviral therapy in Taiwan. *J Infect Dis.* 2004 Sep 1; 190(5): 879-85; Montaner JSG et al. The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic. *Lancet.* 2006 Aug 5; 368(9534): 531-6).

Several groups have now shown through mathematical modeling that further expansion of ARV coverage should lead to lower community-level HIV load (i.e., reducing the total amount of HIV in the community) and thereby dramatically decrease HIV transmission. Evaluating the added preventive impact of expanded access to ARV in LMIC has been identified as a high programmatic priority. This has critical implications from a public health perspective, as well as with regard to the sustainability of the roll out of HAART in this setting. Recent economic modeling suggests that ART becomes cost averting when the impact of this intervention on HIV transmission is considered (Granich, R et al. Universal HIV Testing with Immediate Antiretroviral Therapy as a Strategy for Eliminating HIV Transmission, *Lancet* 26 November 2008).

Initiation:

- **When should ART be initiated and what impact will earlier initiation have on the health care system?**

Since the availability of triple-drug therapy in 1996, experts in the developed world have carefully fine-tuned the optimal initiation of ART. Unlike the consensus that exists for treating chronic HIV infection, the decision to treat acute or early infection varies by individual circumstance and by physician. According to recently updated IAS-USA guidelines, however, the pendulum is swinging back to treating earlier. Released in advance of the International AIDS Conference in Mexico City, the new guidelines take into consideration improved ARV combinations, mounting evidence from several observational trials of the damage to major organs caused by the inflammatory immune response to HIV infection, new longitudinal data from cohort studies, cost effectiveness and potential immunologic and other health benefits in the recommendation to initiate treatment in patients earlier than once established.

In LMICs, the issue of timing is now considered to be one of the most pressing in treatment scale up. In a summary article on when to treat, Dr. Joel Gallant argues that for much of the HIV-infected population, a recommendation to start antiretroviral treatment current guidelines means "little in terms of actual practice," (When to Start Antiretroviral Therapy: A Swinging Pendulum, *IAS-USA Topics in HIV Medicine*, June/July 2008). In fact, in resource-limited settings, where the situation for the diagnosis, treatment and care of HIV is very different, the implications of the updated guidelines remain extremely unclear. The reality is that many individuals enroll in treatment programs late in disease progression, resulting in increases in morbidity and mortality in the first six months of enrollment. Any significant changes, then, to treatment initiation could have an impact on workload and overall resources, and ultimately affect the ability to deliver treatment and care. Feasibility, sustainability and cost-effectiveness of treating early in the LMIC setting, are several issues in particular that will require further examination.

Optimization:

- **What are the most potent, durable and cost-effective first-line and second-line regimens for different populations, including adults, children and injecting drugs users? What and how do clinical, biological and epidemiological factors affect these cost-effective ratios? What are the optimal time, and criteria, for switching to second-line and salvage regimens?**

As more and more individuals gain access to ART through global roll-out initiatives, they will eventually require second line therapy. This will mean significant increases in the cost and burden on national ART programmes and clinical care centres. That said, the availability of 2nd line regimens would bring about enormous benefits at the individual and society level by reducing morbidity and mortality. In addition, new drugs and new drug classes, as well as new formulations, could have a significant impact on recommendations for first and second-line regimens. This is particularly critical with regard to cost and clinical management issues in delivering ART using the public health approach.

Monitoring

- **What is the appropriate role of clinical endpoint and CD4+ and VL monitoring in LMIC, and what formulations could have an impact on adherence, preventing resistance and ensuring the durability of drug regimens in different populations?**

There is mounting evidence that clinical endpoint monitoring alone is sub-optimal for assessing when to switch and can lead to the development of resistant mutations. Resistance is becoming one of the most serious challenges of the HIV epidemic, particularly in LMIC. Knowledge needs to be gathered and shared as to which drug regimens and models of adherence promote increased durability of first-line and second-line regimens and what programmatic factors are associated with the development of virologic failure. The role of laboratory and clinical endpoint monitoring represents an ongoing concern due to limitations on resources and training. As well, the rapid scale-up of ART in LMIC will require an effective pharmacovigilance system to collect information on adverse events that can be used at a programmatic level.

Programme Implementation and Health Systems Strengthening:

- **How can task-shifting, decentralized care, deployment of community health workers and other strategies be used to optimize rollout of ART programmes? How can ART programmes contribute optimally to strengthening of overall health systems?**

Weak health system infrastructure and massive shortages of health care providers are fundamental challenges to rolling out long-term, sustainable treatment programmes. There is mounting evidence that strategies such as WHO's Treat, Train, Retain can have a significant impact in expanding health system capacity for delivering ART to PLHIV in LMICs. Additional research is required to determine the most effective combination of strategies to maximize the delivery of ART programmes in LMICs and have a positive impact on health systems.