

## A CALL TO ACTION FOR THE GLOBAL HIV VACCINE ENTERPRISE

AVAC Report 2007 identifies a number of challenges facing the field, which will be most effectively addressed by collaborative work.

These include:

- The need to foster innovation and independent work, particularly of young scientists, along with “big science”;
- The need to sustain industry involvement;
- The need to anticipate how current vaccine trial results and developments in other prevention fields will influence the size, cost, and goals of future AIDS vaccine clinical trials;
- The need to build better bridges between the AIDS vaccine field and other research and implementation arenas.

We are not alone by any means in calling for greater collaboration. The Global HIV Vaccine Enterprise was founded precisely to create a coordinated response to enduring challenges in the field.

The Global HIV Vaccine Enterprise was proposed in an article authored by 24 leaders in HIV vaccine research and published in *Science* magazine in June 2003<sup>5</sup> (for a timeline of select Enterprise activities to date, see p. 27). The Enterprise was envisioned as a group of independent entities united by a shared commitment to finding an AIDS vaccine. In February 2005, this commitment was further defined with the publication of a Scientific Strategic Plan, which laid out core directions for the field, in *PLoS Medicine*.<sup>6</sup>

Six working groups involving more than 120 participants from 15 countries contributed to this plan, which aimed to provide a blueprint for coordinated work throughout the field. The working group topics were: vaccine discovery,

### AVAC'S ENTERPRISE UPDATE AT A GLANCE

#### AREAS OF PROGRESS

Increased funds flowing into research and selected other areas such as manufacturing and clinical trials aligned with the Enterprise Scientific Strategic Plan

Increased sharing of data and samples through formal agreements at groups like CHAVI and CAVD

Increased understanding of genetic determinants of viral control and slower disease progression from CHAVI

Creating a supportive environment for collaborative work on clinical trials like PAVE 100

#### AREAS WHERE THE CLOCK IS STILL TICKING

Invigorated field-wide analysis and decision-making on critical topics related to clinical trials, regulatory issues and intellectual property

Ongoing analysis of how activities in the field are (and are not) filling identified gaps

Follow up on head-to-head trials, assay standardization and other areas requiring even greater collaboration

Development of a clear independent voice distinct from the Gates Foundation

laboratory standardization, product development and manufacturing, clinical trials capacity, regulatory issues, and intellectual property. The goal of each working group was to provide roadmaps and recommendations for the field as a whole and to identify areas where new or realigned strategy and funding would be likely to improve outcomes.

<sup>5</sup> Klausner, RD, Fauci AS, et al: “The need for a global HIV vaccine enterprise.” *Science* 300:2036, 2003

<sup>6</sup> Coordinating Committee of the Global HIV/AIDS Vaccine Enterprise: “The Global HIV/AIDS Vaccine Enterprise: Scientific Strategic Plan.” *PLoS Medicine*: January 18, 2005 doi:10.1371/journal.pmed.0020025

In the two years since the Plan was published, the Enterprise has had several important accomplishments. The NIH-funded Center for HIV/AIDS Vaccine Immunology (CHAVI) and the Gates-funded Collaboration for AIDS Vaccine Discovery (CAVD) are new collaborative research efforts that unite major players in the field with unique agreements on data and sample sharing, all with the goal of overcoming some of the toughest scientific challenges.

Both CHAVI and CAVD take a “big science” approach to solving enduring problems. In July 2007, CHAVI announced one of the first findings from its work: the “host genetics team,” which is led by David Goldstein (Duke University), published findings from its genome-wide association study. This involved close analysis of nearly 500 DNA samples from HIV-positive people, chosen from a pool of more than 30,000 samples.

Analysis of these samples identified human genes that appear to play a role in how well individuals control HIV and/or remain healthy, without disease progression, in the absence of antiretroviral therapies. This scale of analysis would not have been possible without CHAVI’s collaborative muscle, and CHAVI, in turn, is clearly aligned with the Enterprise and its goals.

Likewise, members of the Partnership for AIDS Vaccine Evaluation, or PAVE, have told AVAC that formation of the Enterprise solidified the collaborative spirit that has brought the NIH, Centers for Disease Control and Prevention, the US Military HIV Research Program, and the International AIDS Vaccine Initiative (IAVI) together to evaluate the Vaccine Research Center’s (VRC) DNA-Ad5 vaccine strategy in the planned PAVE 100 trial.

There are also positive signs that new players are getting involved to tackle gaps specifically identified in the Scientific

Strategic Plan. In February 2007, Canada joined with the Gates Foundation to launch the Canadian HIV Vaccine Initiative, which includes a program on manufacturing that is closely aligned with the needs outlined in the plan. Also recently, the European and Developing Countries Clinical Trials Partnership (EDCTP) and the Gates Foundation launched a joint call for proposals to support capacity building in developing countries.

But for all of these accomplishments, the Enterprise has yet to fulfill its promise.

From its inception, the Enterprise has always made it clear that it was to be the sum of its parts, relying on various partner groups to align their plans with the Scientific Strategic Plan and implement activities towards achieving goals laid out in the shared plan. CHAVI, CAVD, IAVI, Europrise, and others have played key roles in this work.

But the Enterprise has also, at least in theory, promised to be a whole that is *greater* than the sum of its parts. As various players align their work with specific goals, the Enterprise should provide a mechanism for assessing progress and making course corrections if needed. Of course, each research group must measure its own progress against relevant milestones and make course corrections accordingly. But there is also a need for field-wide analysis.

As an example, a recently published report co-funded by the Gates Foundation and IAVI calls for improving the research and development decision-making process and states that “investments in the availability of and use of common procedures across labs, and possibly in head-to-head comparisons of leading candidates” could enhance field-wide decision making on which candidates advance to larger scale trials<sup>7</sup>.

<sup>7</sup> HIV Vaccine Research and Development: Modeling the Path to Speedier Success (2006), International AIDS Vaccine Initiative and the Bill & Melinda Gates Foundation. Available at: [www.iavi.org](http://www.iavi.org)

At present, there is no formal mechanism to move valid field-wide recommendations such as this one into practice—yet it clearly warrants further exploration and refinement. (In the absence of established correlates of protection, it may not make sense for trials to limit themselves to common procedures—but a core set of shared assays could indeed help improve decision-making.)

The Enterprise’s own progress report, published in August 2007, further highlights the need for work to translate recommendations into actions. Its first section summarizes ongoing work in the field; its second covers the key recommendations from three meetings held to address enduring scientific challenges. And yet the reader who was using this document as an introduction to the Enterprise would be hard-pressed to understand whether and how the entities cited in the first section were taking up the recommendations made in the second section.

While this may be a matter of developing a better format for the progress report, it also speaks to the deeper need for the Enterprise to provide updates that refer back to the gaps identified in the plan and so help to track progress from where partners started, to where they are today. The Report does not do this; we look forward to an updated Scientific Plan—which is scheduled for completion in the near future.

This is critical because there has been limited activity in three of the six areas identified in the original plan: clinical trial capacity, regulatory issue considerations, and intellectual property issues.

There is a need for ad hoc groups that bring together key stakeholders in each of these areas to consider emerging challenges. These meetings don’t need to consider all the possible ramifications of a given topic. They need to be targeted and tailored to key challenges, be they questions

**Figure 9. GLOBAL HIV VACCINE ENTERPRISE TIMELINE 2003-07\***

2003	2004	2005	2006	2007
Enterprise concept paper published in <i>Science</i>	6 Working groups convened: vaccine discovery, laboratory standardization, product development & manufacturing, clinical trials capacity, regulatory issues, intellectual property	Scientific strategic plan published in PLoS medicine	Announcement that Adel Mahmoud would not assume role as Enterprise Executive director	Meetings held on topics including trial design, humoral and mucosal immunity
Airlie House meeting to develop Enterprise concept		Stakeholders meeting, London		Enterprise publishes first report on its activities
		NIH awards for CHAVI to Duke University	Gates Foundation announces grants for CAVD	
		Funders’ Forum, London		

\* Adapted from Global HIV Vaccine Enterprise: Report of Activities 2005-2007 (2007)

about how changes in standard of prevention will impact trial size, funding, and capacity needs, or how lack of clarity on international intellectual property might cause roadblocks for future product development.

The Enterprise is well-positioned to convene such groups, and its initial scientific plan suggested that these would be key areas of work. If that has shifted, then the plan should be updated accordingly—the key to the success of the Enterprise is not to be all things to all people, but to be clear about its role and goals.

Hiring an executive director should accelerate progress on these goals. A leader who has a strong and, where necessary, challenging voice could help to initiate discussions on specific high-priority topics and follow through on key recommendations that emerge from these and other meetings. He or she could help to move the Enterprise into a second phase—one that uses the collaborative spirit and initial work of the first two years as the foundation for an expanded, ambitious scope of work.

A new executive director could also help the Enterprise to develop an identity that is distinct from the Gates Foundation. The Foundation has housed a small Enterprise secretariat since 2005, which has worked energetically to move the Enterprise forward.

In its next phase though, the Enterprise should move in a more independent direction. The global perception that the Gates Foundation has “taken care” of investments in HIV-prevention research is false, yet persistent. With a strong director at the helm, the Enterprise secretariat will be able to tackle fundraising, if needed, and, we hope, to be both a critical and a unifying voice.

## **AVAC sees four critical action areas for the Enterprise and its incoming Executive Director in 2008:**

### **1. Implement collective planning and decision-making on product candidate advancement**

The AIDS vaccine field faces multiple, critical decisions about which products to move forward and when. Though there has been discussion for years about the need for head-to-head trials of candidates, it has not happened.

### **2. Translate Enterprise 2007 report recommendations into specific action plans**

The current report on the Enterprise summarizes activities in the field and makes recommendations for filling gaps in some critical areas. The updated Scientific Strategic Plan should place these recommendations into the “big picture” of Enterprise activities and identify new or persistent gaps.

### **3. Address clinical trial capacity issues**

There is a clear need for resources and strategic thinking around clinical trial capacity development, including expanding infrastructure and human resources (scientific leadership from developing countries, counselors, laboratory technicians, recruitment staff, and others). The EDCTP plays part of this role, but a single entity working alone cannot solve the global issues. In 2008, the Enterprise should convene focused discussions on clinical trials to develop a strategic plan and operational action recommendations.

### **4. Engage a broader range of community stakeholders**

AVAC has been committed to working with the Enterprise since its inception, attending the Airlie House meeting in 2003 and contributing to development of the Scientific Strategic Plan. But we do not and cannot represent the full

scope of community issues and perspectives for the world. The Enterprise should ensure representation from all key constituencies and community stakeholders and should actively support capacity building for prevention research advocacy worldwide.

AVAC recognizes the tension in our own role as watchdog of both the Enterprise and the Gates Foundation, given that we receive funding from both the Enterprise secretariat and the Gates Foundation. We are a member of the Enterprise, and Bill Snow, a co-founder and board member emeritus of AVAC is on the Enterprise coordinating committee. We recognize the challenges this brings to our work and we are committed to independence of thought and advocacy. We are all learning as we go.

The newly-published Enterprise report tells us that it will be January 2008 when the Executive Director takes on the job. It takes time—often a year or more—for a new leader to get up to speed, develop a plan of action, and find the right staff.

AVAC believes that the vaccine field cannot afford to wait another year for the Enterprise to run on all cylinders. Therefore, we call on the Enterprise partners and the interim secretariat to start getting ready for the incoming director. Specifically:

- Begin the preparatory work to revise and publish an updated scientific strategic plan including a gap analysis and recommendations to the partners, the new leadership, and the science strategy committee.

- Consult key stakeholders to identify high-priority, under-discussed topics in the areas of clinical trial capacity, manufacturing, and intellectual property; and to convene focused meetings to consider specific questions and generate recommendations that can be used to inform the ED's first year of work.
- Develop an Enterprise business plan with specific milestones for the next two years, including a transparent process for monitoring timelines and results. The incoming ED should review, modify, and publish this during the first quarter of 2008.

The Enterprise was conceived as a global collaboration to add strategy and urgency to the search for an effective AIDS vaccine. While a single leader cannot and should not be the sole focal point of the endeavor, the time is well past for this critical effort to have an independent voice, a face, an outspoken champion. AVAC looks forward to collaborating with the Enterprise leadership in communicating the growing urgency of the need for a vaccine and in instituting policies and practices to ensure that research and development, and trial processes are continually improved and accelerated.