



Global HIV Vaccine Enterprise

The Funders' View

On July 10, 2014, the Global HIV Vaccine Enterprise held its third annual Funders' Meeting, a gathering of the major funders of HIV vaccine research and development, in Washington, DC. The meeting brought together individuals representing the gamut of funding organizations, not quite from A to Z but from A to V (see participant list at right), to discuss updates to their programs and to explore common themes that may inform future funding decisions, determine how to best align available resources, promote collaboration, and guide the Enterprise in fulfilling its mission.

This report provides a high-level perspective of the daylong meeting, including a summary of key research priorities of the funding organizations, changes to funding mechanisms that are underway, and some of the areas for closer collaboration.

Research Priorities

All twelve organizations present at the meeting shared their research priorities. Because of their size and scope, programs from two organizations tend to significantly influence HIV vaccine research and development: the US National Institutes of Health (NIH), and the Bill & Melinda Gates Foundation (The Gates Foundation). As a result, the NIH and the Gates Foundation largely tend to drive the research priorities for the field and work closely together to invest in everything from

Organizations Represented at the 2014 Funders' Meeting

(in alphabetical order)

AVAC: Global Advocacy for HIV Prevention
Bill & Melinda Gates Foundation
Canadian HIV Vaccine Initiative
European Commission
European & Developing Countries Clinical Trials Partnership
International AIDS Vaccine Initiative
National Institute of Allergy and Infectious Diseases, NIH
Office of AIDS Research, NIH
Public Health Agency of Canada
UK Medical Research Council
UNAIDS, the Joint United Nations Programme on HIV/AIDS
United States Agency for International Development
U.S. Military HIV Research Program
Vaccine Research Institute, France

basic discovery to clinical research. Other funders strengthen these efforts by taking advantage of their unique strengths and capabilities, as described below.

The NIH supports a variety of HIV-vaccine related research that ranges from unsolicited, investigator-initiated projects to large consortia, including two Centers for HIV/AIDS Vaccine Immunology — Immunogen Discovery (CHAVI-ID), and the components of the HIV Vaccine Trials Network (HVTN). It also conducts intramural research at NCI and NIAID, including the Vaccine Research Center (VRC). The Gates Foundation's major investment is the Collaboration for AIDS Vaccine Discovery (CAVD), a constellation of consortia linked by use of shared

Continued on the next page...

Toward a Cure

Another research priority discussed is the increasing intersection of preventive vaccine research and functional cure efforts with immune-based interventions, such as use of monoclonal antibodies and therapeutic vaccines. Emerging science in this area is driving funders to explore synergies between these once separate endeavors.

central service facilities, enabling standardization of key assays as well as sharing of data and materials.

One area of basic research undergoing a renaissance is non-human primate (NHP) research, with multiple new hybrid SIV/HIV viruses (SHIVs) under development that will enable improved preclinical evaluation of vaccine candidates. Two Simian Vaccine Evaluation Units (SVEUs) aim to study mechanisms of protection of vaccines in NHPs.

Antibodies are another priority area of basic research, with funding going to projects that attempt to design immunogens to elicit broadly neutralizing antibodies (bNAbs) against HIV (the Gates Foundation funded IAVI Neutralizing Antibody Consortium plays an important role here), improve durability of antibody responses induced by vaccination, and elucidate the role non-neutralizing or so-called “functional” antibodies play in protection.

Funders are also focusing on alleviating what some view as a major obstacle to developing antibody-based vaccine candidates—the current shortage of HIV Envelope (Env) protein immunogens available for testing in clinical trials. One important aspect of this work is to create the capability to manufacture a variety

of small batches of Env protein to be tested in phase I or exploratory medicine trials. The main goals are to manufacture these proteins quickly and to reduce costs, but funders also recognize the need for better protein analytics and increasing yields in manufacturing through improved expression platforms and purification systems. The Gates Foundation is establishing a virtual Analytics Core to facilitate analysis of purified proteins and protein-adjuvant formulations and NIAID is issuing an RFP in this area. Meanwhile, the Gates Foundation is expanding its funding for the IAVI-based Vaccine Product Development Center, which assists CAVD researchers in readying a variety of candidates for clinical evaluation. They are also interested in using replicating viral vectors that present HIV Env in its native conformation.

In clinical vaccine research, the top priority for HVTN is the efficacy trials in South Africa that are part of the Pox Protein Public-Private Partnership (P5) formed to follow-up on the limited efficacy afforded by the canarypox viral vector/protein prime-boost strategy tested in the RV144 trial in Thailand.

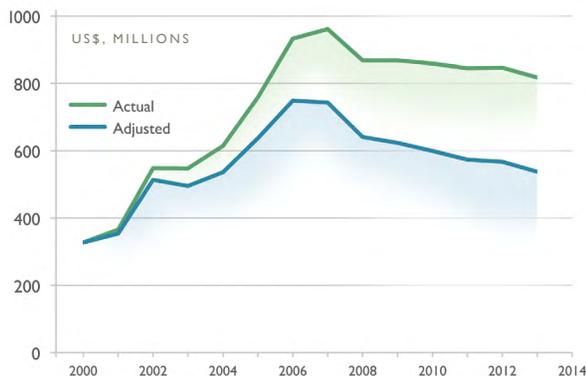
Passive immunization with bNAbs is an area of considerable interest as it may inform active vaccination strategies. The Vaccine Research Center at NIAID with its antibody VRC01 is leading efforts on the prevention front with clinical testing of their VRC01 antibody, while Rockefeller University is evaluating two bNAbs for treatment/functional cure.

While the above summary captures a high-level update of research efforts primarily from the NIH and the Gates Foundation, all of the funders present at the meeting shared their priorities and provided updates on planned modifications to their portfolios. Highlights of the major changes anticipated in HIV vaccine funding streams as well as some of their research priorities are listed below, in alphabetical order by funding organization:

- The [European Commission](#) recently launched the new EU funding program for research and innovation, Horizon

HIV Vaccine Funding Declines

Worldwide Investment in HIV Vaccine R&D



ADAPTED FROM [HTTP://WWW.HIVRESOURCETRACKING.ORG](http://www.hivresourcetracking.org)

The HIV Vaccines and Microbicides Resource Tracking Working Group released its 10th annual report in July showing HIV vaccine funding fell to US \$818 million in 2013 from US \$847 million the previous year. After adjusting for inflation, (using the NIH's Biomedical Research and Development Price Index), funding levels dropped 28% in 2013 from their highest level in 2006. Given this funding environment, there is a strong commitment to optimize use of existing resources, improve collaboration, and align the funders' priorities, and this emerged as a broad theme at this year's Funders' Meeting.

2020 (H2020), where prevention remains a high research priority as well as HIV/AIDS. H2020 supports all steps of product development, from discovery to clinical trials and capacity building, with the use of different funding instruments (including EDCTP2). In H2020, there is currently an open call for proposals that would shift the 'risk curve' of development by improved selection of successful vaccine candidates at earlier stages of the vaccine development process. In addition, the second phase of the Innovative Medicines Initiative (IMI-2), a partnership between the private (EFPIA) and the public (European Commission), was launched in 2014. The IMI-2 strategic agenda includes vaccine research and represents an important funding opportunity for HIV research on topics where industry is willing to commit in-kind resources to collaborate with the public sector.

- The first iteration of the [European & Developing Countries Clinical Trials Partnership](#) (EDCTP) is coming to an end, and EDCTP 2 will begin with a mission to support clinical trials of all phases for an expanded scope of neglected diseases, and will also fund research on the optimization of health services.
- [IAVI](#) is striving to build scientific leadership and ownership of HIV vaccine research in Africa and to leverage its network of clinical research centers there by involving them in the design and testing of vaccine candidates.
- In addition to participating in the P5 efforts, [MHRP](#) is planning to advance a modified vaccinia ankara/adenovirus serotype 26 (with mosaic gag/pol/env inserts)/gp140 foldon

protein prime-boost strategy into clinical trials. They also plan to capitalize on their early infection cohorts to study the potential of early treatment with antiretrovirals, antibodies, or therapeutic vaccine candidates to improve treatment responses, or potentially even achieve a functional cure.

- Created in 2011 as a virtual program bringing together 17 teams, [Vaccine Research Institute](#) in France is focusing on DC-based vaccines and is testing a portfolio of candidates in NHPs and in Phase I and II clinical trials.
- In accordance with its mission, [USAID](#) plans to focus primarily, but not exclusively on downstream research in areas of high HIV prevalence in Africa and India, as they prepare for the next set of awards to enable more partnership opportunities.

Areas of Common Interest

Almost unanimously, representatives of the major funding organizations expressed a desire to share more information across all areas, which would allow funders to develop a shared sense of where the gaps in funding are and also to optimize allocation of existing resources (see HIV Funding Declines). Consensus emerged on three main areas that could benefit from better collaboration.

Regulatory Capacity

Funders emphasized the need to better understand and map existing regulatory capacity in developing countries

Continued on the next page...

“The funders are really the core of the Enterprise.”

Bill Snow, Director of the Global HIV Enterprise

to see where gaps exist. Many organizations are already trying to improve regulatory capacity and provide training, and information on ongoing and planned efforts in this area would help all stakeholders more effectively achieve their goals.

Clinical Trials Capacity

IAVI, the EDCTP, and the HVTN lead the efforts in tracking HIV incidence, identifying and sustaining clinical trial sites, and monitoring the impact of access to other prevention and treatment modalities. A more coordinated effort to map and share information on clinical trial site capacity across the broad network of prevention trials funders was suggested. The World RePORT database (<http://worldreport.nih.gov>) gathers information from international funders of biomedical research in Africa, and could be used to highlight where clinical research capacity or epidemiology strengths exist. Although sufficient capacity to conduct clinical trials exists at this time, there is a concern that more will be needed in the future as more vaccine candidates move forward into advanced testing in parallel or together with other HIV prevention options. There are also concerns that certain sites may be affected if candidate vaccines with appropriate clade specificity are not available for testing.

Don't Forget the Social Science

Funders emphasized the importance of integrating social and behavioral research into HIV vaccine discovery efforts with an eye toward improving recruitment and retention of volunteers in clinical trials, and understanding both the perception of and interest in combination prevention.

Manufacturing

There was broad consensus given the high-priority, yet very expensive work of manufacturing clinical grade material approved for human trials, that this was an area where better coordination among funders could ensure that available funding is used most efficiently. Specifically, funders highlighted the need to coordinate approaches to identify and manage contract manufacturers, jointly prioritize what is manufactured, and to share lessons learned on technical and regulatory aspects.

Conclusion

While many of the funders are already working together and there is a willingness to share information, those funders present at the meeting agreed that improving collaboration and communication in the areas listed above as well as and other areas will allow funders to join efforts, avoid duplication of effort, and more effectively address critical needs.

In summary, the funders stressed the value of platforms like the Funders' Meeting as a venue for identifying common concerns and to discuss different approaches to addressing them.



GLOBAL HIV VACCINE ENTERPRISE
VACCINEENTERPRISE.ORG
INFO@VACCINEENTERPRISE.ORG