

AIDS Vaccine 2007, Seattle, August 20-23, 2007



Global HIV Vaccine
Enterprise

THE ENTERPRISE: PROGRESS AND CHALLENGES

José Esparza

Promoting innovation and collaboration
to speed the search for an HIV vaccine

- + **2003: Conceptualization**
 - + Proposal in *Science*
 - + Definition of vision
- + **2004: Planning**
 - + Scientific plan
 - + G8 endorsement
- + **2005-06: Early Implementation**
 - + Center for HIV/AIDS Vaccine Immunology (CHAVI)
 - + Collaboration for AIDS Vaccine Discovery (CAVD)
- + **2007 & beyond: Coordination and Expansion**
 - + EDCTP and Canada contributions
 - + Establishment of the permanent Secretariat
 - + New Enterprise activities and stakeholders

POLICY FORUM

MEDICINE

immune effector mechanisms are responsible

The Need for a Global HIV Vaccine Enterprise

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tematically more candidate vaccines. Despite the wide variety of conceptual approaches to HIV vaccine design, the pace of development of new HIV vaccine candidates needs to be accelerated. In 2001 and 2002, only seven immunogens entered clinical trials. Only one candidate vaccine, aimed at eliciting neutralizing antibodies to a soluble HIV envelope protein, entered human phase III testing. Unfortunately, the recently released results from this trial did not demonstrate vaccine efficacy in the overall trial cohort (2). Although many approaches to producing immunogens have been discussed and initiated, systematic evaluation and optimization have proceeded slowly, in part because of factors such as the expense and complexities in advancing new candidate vaccines into phase I trials and scientific challenges.

These challenges include (i) the inability of current vaccine designs to elicit effective neutralizing antibodies against the circulating strains of HIV, (ii) the inability of current designs to prevent HIV from establishing persistent infection, (iii) the extensive global variability of HIV, (iv) the lack of understanding regarding the mechanisms of protection in the most effective HIV vaccine animal model system—the live attenuated approach, and (v) the lack of understanding of which HIV antigens induce protective immunity and which im-

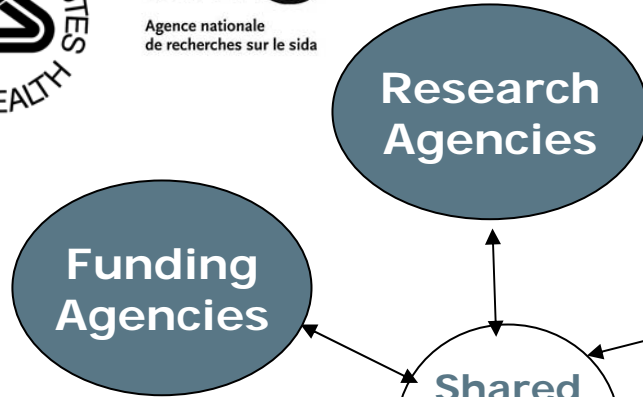
prove empiric and iterative, building on sequential successes to define correlates of immune protection that guide product development. Preclinical and clinical experiments and evaluation systems with objective measurements and analysis have been critical. Perhaps one of the most successful examples of such a concerted, empiric approach in medicine generally is the improvement in the treatment of childhood acute lymphocytic leukemia (ALL). Cure rates for children with ALL have improved from ~10% in the 1950s to more than 80% (and for some subtypes, 100%) in 2002. This increase has been produced almost entirely by a coordinated and iterative series of preclinical drug evaluations and subsequent clinical trials, in which partially effective drug regimens have been systematically altered (through studies of the effects of combination and sequence), to produce steady and significant improvement in survival as well as reduced toxicity.

HIV vaccine development has several similarities with developing treatment for ALL: (i) Although animal model data provide major conceptual insights, human clinical trials are ultimately required to define vaccine or drug effectiveness; (ii) the number of possible variables in reagent design and clinical outcome are large but definable; (iii) combinations of reagents

The Enterprise is all of us



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CHIRON | VACCINES



sanofi pasteur
The vaccines business of sanofi-aventis Group



+ Developed by 140 scientists from 15 countries

Published in PLoS Medicine, February 2005

+ Six priority areas:

- Vaccine discovery
- Laboratory standardization
- Product development and manufacturing
- Clinical trials capacity
- Regulatory issues
- Intellectual property

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Policy Forum

The Global HIV/AIDS Vaccine Enterprise: Scientific Strategic Plan

Coordinating Committee of the Global HIV/AIDS Vaccine Enterprise

Introduction

In June 2003, an international group of scientists proposed the creation of a Global HIV Vaccine Enterprise [1]. The authors invited discussion of this proposal, and challenged scientists to identify new strategies and mechanisms to accelerate the global effort to develop a safe and effective HIV vaccine. This paper describes the processes that led to agreement on the major roadblocks in HIV vaccine development, summarizes current scientific priorities, and describes an initial strategic approach to address those priorities. Specific research is not prescribed. Rather, the intent is to stimulate both researchers and funders to explore new, more

include an expanded HIV vaccine candidate pipeline, improvements in animal models, a growing database from clinical trials, and the availability of new quantitative laboratory tools that make comparisons among vaccine studies feasible. Confronting major roadblocks and harnessing these new opportunities requires an effort of a magnitude, intensity, and design without precedent in biomedical research, with the Human Genome Project as a potentially useful model [4]. More specifically, the critical scientific insights generated by the creativity of individual groups be significantly organized in the design of novel interventions. These interventions provide groups, and their design in knowledge support decision vaccine and clinical success. The Enterprise seek an development of developing creating address. The Enterprise efforts: common help en sources approach global c more of suring t

The major difficulties encountered in the development of an HIV vaccine are scientific, not organizational.

collaborative, cooperative, and transparent approaches to address the major obstacles in HIV vaccine development identified in the plan, in addition to continuing the productive, high-quality programs already underway.

The motivation behind the proposal for a Global HIV/AIDS Vaccine Enterprise was the recognition that development of an HIV vaccine remains one of the most difficult challenges confronting biomedical research today [2,3]. Fortunately, scientific progress has created new opportunities that could be harnessed more effectively through global coordination and collaboration. These new opportunities

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Asthma on the rise
HIV vaccine strategy
Pathway to diabetic nephropathy

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What the Enterprise plan is – and is not

- + The plan was developed as an exercise in consensus building, making broad suggestions in different areas in the HIV vaccine R&D continuum, providing a road map that funding and research agencies can use to plan or align some of their activities in a coordinated fashion
- + The plan is not prescriptive (it is not a check list of “things to do”) and does not include every HIV vaccine activity. It focuses on those areas that require increased collaboration and coordination
- + The plan aims to describe a research agenda that is broad enough to attract brilliant people to explore new avenues, but at the same time maintain the focus on the applications of the research
- + Following the model of the Human Genome Project, during the first years of the Enterprise the plan should have enough flexibility to explore the “things we don’t know that we don’t know”
- + In subsequent years, when science and coordination mature, at least some of the areas of the scientific plan will become more targeted and specific



CHAVI
CENTER FOR HIV/AIDS VACCINE IMMUNOLOGY

- + Launched in 2005, CHAVI is a consortium of scientists trying to solve major problems in HIV vaccine development and design through the work of 10 highly collaborative Discovery Teams supported by 12 cores.
- + CHAVI now involves 95 investigators in 36 institutions in 8 countries.

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- + Launched in 2006, the CAVD is a highly collaborative network of 16 research consortia, comprising more than 180 investigators, in almost 90 institutions, in 22 different countries.
- + 11 of the consortia are working on different approaches developing HIV vaccines and the other 5 provide standardized evaluation of immune responses, data analysis and statistical support, and storage and distribution of samples.



- + Expanded its Neutralizing Antibody Consortia (NAC), created a consortium to address correlates of immunity, and established an AIDS Vaccine Development Laboratory.
- + With support from the Gates Foundation IAVI will soon launch an innovation program focusing on the biotech sector (as part of a broader effort of the Gates Foundation to support innovative research).



- + Preparing for community engagement and revising ethical guidelines
- + Supporting the further development of the African AIDS Vaccine Programme (AAVP).
- + Involved in the Enterprise Coordinating Group and its related activities to prepare for the release of results of ongoing HIV vaccine efficacy trials.



- + The European Commission (EC) is supporting several cooperative HIV research projects, including the EUROPRISE network, that brings together vaccine and microbicide researchers.
- + The European Developing Countries Clinical Trials Partnership (EDCTP) is strengthening clinical trials capacity through multi-center projects in Africa (including a joint call for proposals in collaboration with the Gates Foundation).



- + The Wellcome Trust supports a variety of HIV vaccine research projects consistent with priorities identified in the Enterprise Plan.
- + Currently discussing collaboration with the Gates Foundation to create a supportive environment to explore innovative approaches for HIV vaccine research.



- + The French Agency for Research on AIDS (ANRS) is funding a variety of HIV vaccine approaches within the scope of the Enterprise Plan.



- + The AIDS Vaccine Advocacy Coalition (AVAC) provides policy, advocacy and community perspectives to help connect civil society to the work of the Enterprise.

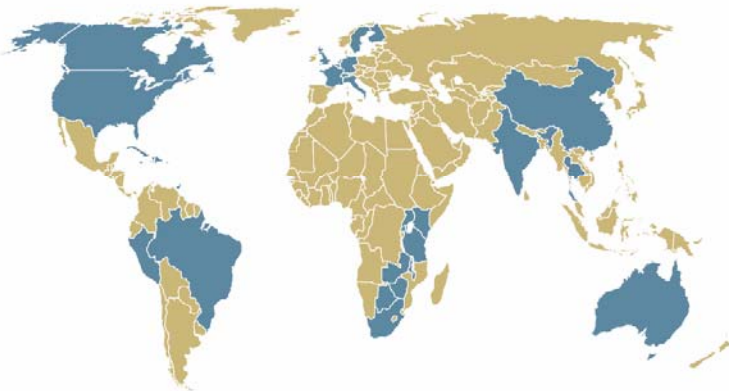


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- + In February 2007 the Government of Canada and the Gates Foundation agreed to collaborate on a new Canadian HIV Vaccine Initiative being developed to support the implementation of the Enterprise Plan, including the establishment of a manufacturing facility for clinical lots for early clinical trials.



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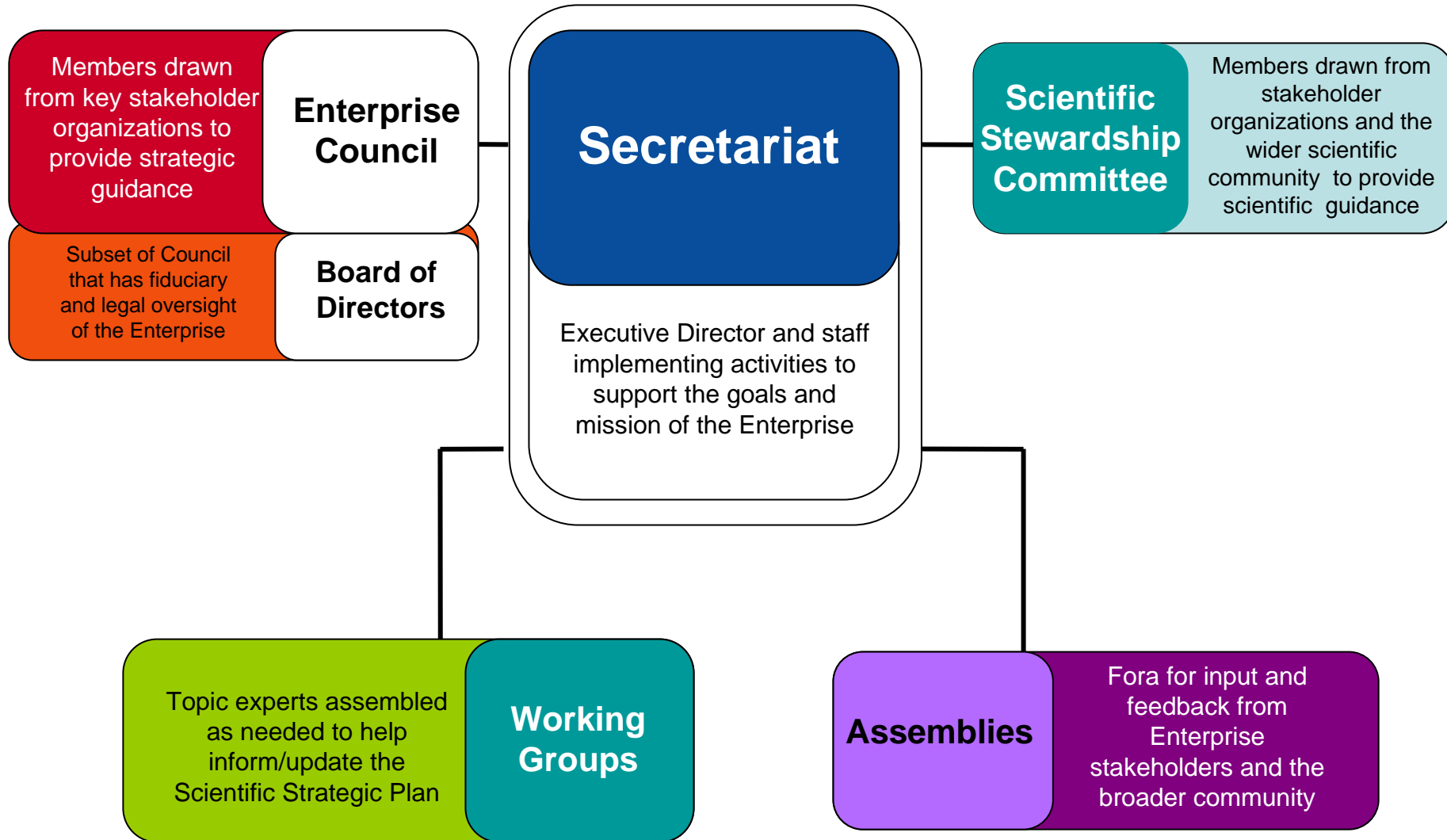
Report of Activities 2005 – 2007

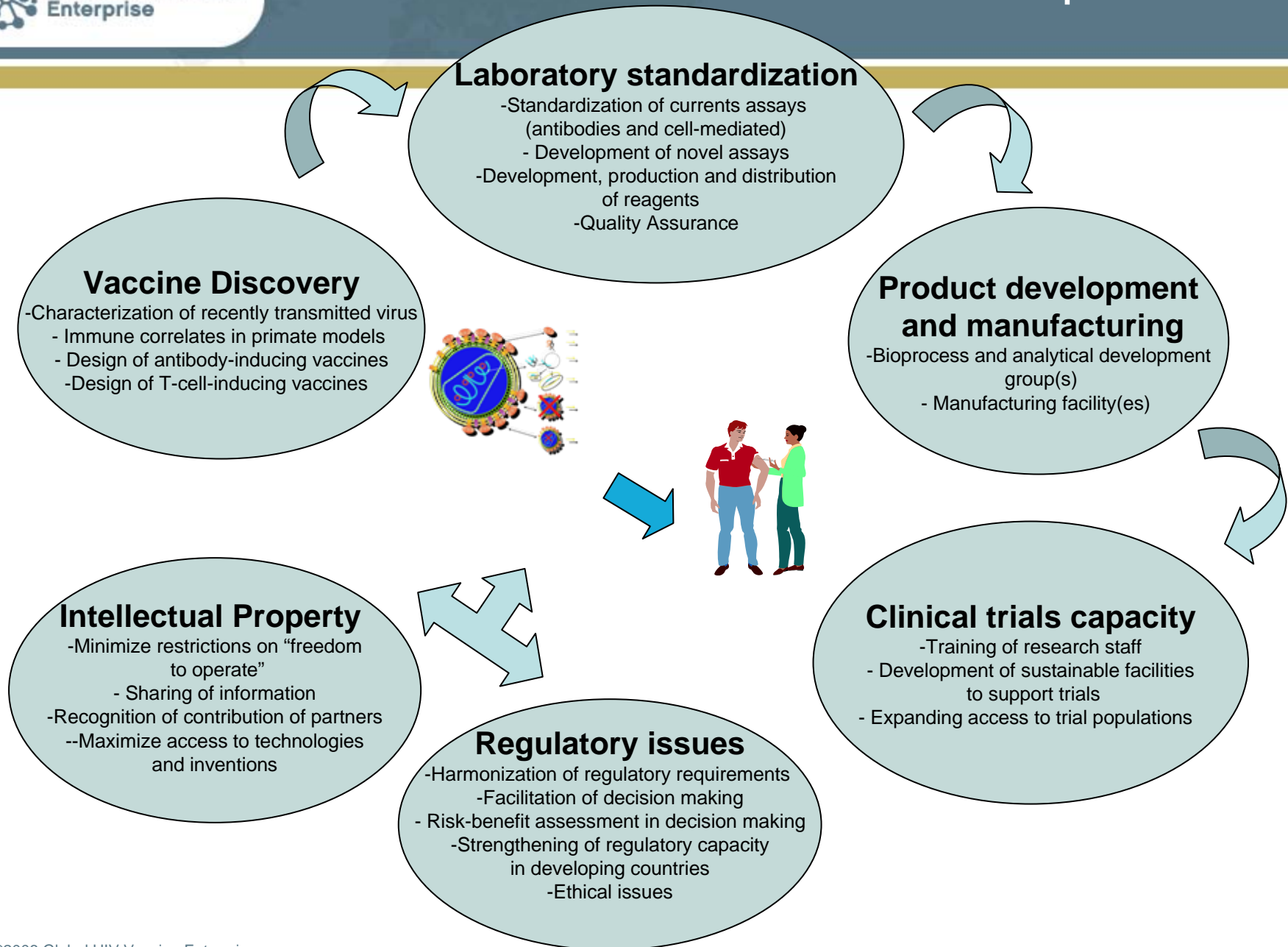


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The Enterprise Structure





- + **Reports from Enterprise Working Groups—Emerging issues in:**
 - + **Humoral response to HIV and approaches to the design of antigens that induce neutralizing and other potentially protective antibodies (David Montefiori)**
 - + **Improving defenses at the portals of entry: innate and mucosal immunity (Robin Shattock)**
 - + **Innovative trial designs to expedite vaccine efficacy evaluation (Nina Russell)**
- + **The as-yet unrealized potential of the Enterprise (Bill Snow)**



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