

THE CANADIAN HIV VACCINES PLAN

TOWARDS A WORLD WITHOUT AIDS



Acknowledgments

Towards a World Without AIDS: The Canadian HIV Vaccines Plan was made possible thanks to the participation of many individuals and representatives of organizations and governments as well as the funding support of the Public Health Agency of Canada.

Thanks are also extended to the members of the Steering Committee who directed the development of this report. Their valuable input and guidance are greatly appreciated.

To obtain additional copies, please contact:

Canadian HIV/AIDS Information Centre
400-1565 Carling Avenue
Ottawa, Ontario K1Z 8R1
Telephone: 1-877-999-7740
E-mail: aidssida@cpha.ca

This publication is also available online at
<http://www.aidssida.cpha.ca>

© Canadian Public Health Association, 2006

ISBN 1-894324-37-4

This document is published by the Canadian Public Health Association on behalf of the stakeholders involved in the Canadian response to HIV/AIDS. The views expressed herein do not necessarily represent those of the Canadian Public Health Association.

July 2006

TABLE OF CONTENTS

List of Acronyms	02
Origins of <i>Towards a World Without AIDS: The Canadian HIV Vaccines Plan</i>	03
The Purpose of the Canadian HIV Vaccines Plan	03
A Call for Action	04
Vision	04
Values	05
Why Does Canada Need an HIV Vaccines Plan?	06
1. The world needs HIV vaccines	06
2. Canada can make a difference	09
Elements of a Canadian HIV Vaccines Plan	15
Components/Strategies	15
1. Discovery:	
Take an integrated strategic approach to HIV vaccine research and development	17
The Challenges	17
The Strategy	19
2. Trials and Testing:	
Enhance Canada's capacity to conduct vaccine trials	21
The Challenges	21
The Strategy	23
3. Production:	
Develop Canada's capacity to manufacture vaccines	25
The Challenges	25
The Strategy	27
4. Distribution:	
Ensure equitable access to HIV vaccines at home and abroad	29
The Challenges	29
The Strategy	30
5. Community Engagement:	
Engage Canadians in vaccines research, production and distribution	33
The Challenges	33
The Strategy	36
6. Political Leadership and Financial Commitment:	
Provide long-term, dedicated leadership and funding	39
The Challenges	39
The Strategy	41
Appendix A	42

ACRONYM LIST

ARV	antiretroviral
CAB	community advisory board
CANVAC	Canadian Network for Vaccines and Immunotherapeutics
CAS	Canadian AIDS Society
CFI	Canadian Foundation for Innovation
CHIVE	Canadian HIV Vaccine Enterprise
CIDA	Canadian International Development Agency
CIHR	Canadian Institutes of Health Research
CTN	Canadian HIV Trials Network
DFAIT	Department of Foreign Affairs and International Trade
F/P/T AIDS	Federal/Provincial/Territorial Advisory Committee on AIDS
G8	Group of Eight
HAART	highly active antiretroviral therapies
IAVI	International AIDS Vaccine Initiative
ICID	International Consortium for Infectious Disease
IDRC	International Development Research Centre
NGO	non-governmental organization
NIH	National Institutes of Health (United States)
PASS	post-approval surveillance system
R&D	research and development
SARS	severe acute respiratory syndrome
SSPE	Subacute sclerosing panencephalitis
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNGASS	United Nations General Assembly Special Session on HIV/AIDS
WHO	World Health Organization

ORIGINS OF THE CANADIAN HIV VACCINES PLAN: TOWARDS A WORLD WITHOUT AIDS

This document is the result of a collaborative process involving researchers, government and the community. In June 2003, Health Canada convened a round-table meeting on HIV vaccines to lay the foundation of a Canadian plan for the development and equitable distribution of HIV vaccines. The round table, which included representatives of Health Canada (Centre for Infectious Disease Prevention and Control, Division of Immunology and Respiratory Infections, and the International Affairs Directorate), the Canadian International Development Agency (CIDA), the Canadian Institutes of Health Research (CIHR), the Federal/Provincial/Territorial Advisory Committee on AIDS (F/P/T AIDS), the Canadian HIV/AIDS Legal Network, the Canadian AIDS Society (CAS), the International AIDS Vaccine Initiative (IAVI), the Canadian Network for Vaccines and Immunotherapeutics (CANVAC), and the British Columbia Centre for Excellence in HIV/AIDS – Canadian HIV Trials Network (CTN), reached consensus on the components of a Canadian HIV vaccine plan.

3

In December 2003, a second round-table meeting was held to develop an outline for the plan and discuss next steps, and to establish a small Canadian Vaccines Plan Steering Committee.

In 2004-05, the Steering Committee developed this document, or road map, for broader consultation. The goal was to engage a larger group of stakeholders and use the road map to develop a comprehensive Canadian HIV vaccines plan. The consultation was conducted in the summer of 2005 with a range of Canadian experts in HIV vaccine development.

The following pages set out some elements of a Canadian HIV vaccines plan, as well as the issues that a comprehensive plan should address.

THE PURPOSE OF THE CANADIAN HIV VACCINES PLAN

Canada has the expertise, experience and resources to make a significant contribution to the global effort to develop HIV vaccines and deliver them to all people who need them, including Canadians. The Canadian HIV Vaccines Plan outlines Canada's contributions to this effort and articulates the vision for Canada's involvement throughout. Specifically, the Plan aims to:

- ✕ Define Canada's role in developing and distributing HIV vaccines.
- ✕ Enhance Canada's capacity to participate in domestic and international efforts to develop, produce and distribute HIV vaccines and to build knowledge of HIV vaccines across all sectors.
- ✕ Develop the sustained public and government commitment required to support an HIV vaccines program.
- ✕ Help guide the allocation of Canadian resources for preventive and therapeutic HIV vaccines, both domestically and internationally.

Canada has many key strengths that it can and should contribute to global efforts to develop and deliver HIV vaccines, including strong community-based organizations; a strong research capacity; immune-monitoring capability; long-term relationships with research partners in the developing world; infrastructure in Canada and internationally;

recognition of our strengths in social science, legal issues and human rights; new possibilities for production plants; emerging private-public sector partnerships; international recognition for our diplomacy; and a strong health care or medical care (medicare is U.S.) system.

The Canadian HIV Vaccines Plan identifies a range of strategies designed to address the six key components of effective HIV vaccine development:

- 1. Discovery:** Take an integrated strategic approach to HIV vaccine research and development
- 2. Trials and Testing:** Enhance Canada's capacity to conduct vaccine trials
- 3. Production:** Develop Canada's capacity to manufacture vaccines
- 4. Distribution:** Ensure equitable access to HIV vaccines at home and abroad
- 5. Community Engagement:** Engage Canadians in vaccines research, production and distribution
- 6. Political Leadership and Financial Commitment:** Provide long-term, dedicated leadership and funding.

The ongoing challenges for Canadian researchers, clinicians and people living with or at risk of HIV/AIDS are to advocate for all populations in Canada affected by HIV – people living with HIV/AIDS, gay men, people who use injection drugs, women, people from countries where HIV is endemic, Aboriginal people – to be informed about and have an opportunity to participate in future trials and to ensure that any clinical trial conducted in Canada or conducted by Canadian researchers in another country offers some long-term tangible benefits for target communities. While the Canadian government has made several related commitments, it has yet to fund a targeted domestic effort building on Canada's human resources, which span researchers, clinicians, community-based organizations, people living with HIV/AIDS, the private sector and policy makers.



"I have a pretty good sense of how incredibly tough the slog will be towards the discovery of a vaccine. We know that when all is said and done, a vaccine is the ultimate answer to this devilish pandemic, and when all is said and done, human ingenuity will one day trump the Machiavellian mutation of the virus. It always does."

Remarks by Stephen Lewis,
UN Special Envoy for HIV/AIDS in Africa
AIDS Vaccine 2005 International Conference

Delivered at the opening ceremony,
Montreal, Canada, September 6, 2005

A CALL FOR ACTION

The HIV/AIDS pandemic is an unprecedented global crisis. HIV/AIDS is today's greatest threat to continued social and economic development; it is devastating many developing countries around the world. The pandemic has dramatically reversed many of the development gains that governments and civil society have worked for decades to achieve. Given the growing threat HIV poses to human life, health and security, we are obligated to make more intense efforts to prevent HIV. An effective response to HIV/AIDS requires coordinated and concerted collaboration across communities, nations and regions and through all sectors. Canadians must act to the greatest possible extent, as global citizens and as a multicultural society. We have an important leadership role to play in marshalling an effective response, both nationally and globally. ∞

VISION

Canada will contribute to global efforts to develop safe and effective preventive and therapeutic HIV vaccines that are accessible to all people living with HIV/AIDS and populations at risk, both in Canada and around the world.

Purpose of this Plan

Canada has the expertise, experience and resources to make a significant contribution to the global effort to develop HIV vaccines and deliver them to all people who need them, including Canadians. The purpose of this plan is to articulate the vision for Canada's contributions across all parts of the effort, including the following components: discovery, trials and testing, production, distribution, community engagement, and leadership. Specifically, this plan aims to:

- ∞ Define Canada's role in developing and distributing HIV vaccines.
- ∞ Enhance Canada's capacity to participate in domestic and international efforts

to develop, produce and distribute HIV vaccines and to build knowledge of HIV vaccines across all sectors.

- ✘ Develop the sustained public and government commitment required to support an HIV vaccines program.
- ✘ Help guide the allocation of Canadian resources for preventive and therapeutic HIV vaccines, both domestically and internationally.

VALUES

This plan is guided by the values articulated in *Leading Together: Canada Takes Action on HIV/AIDS (2005-2010)*.¹

Global Responsibility. As citizens of a caring and affluent nation, we have an ethical responsibility to contribute our fair share of skills and resources to domestic and global efforts to develop and distribute HIV vaccines. We also have a legal obligation under human rights law and treaties to cooperate with other countries to protect health. We will use our strengths to contribute to international as well as domestic HIV vaccine initiatives.

Human Rights. Every person – regardless of factors such as sexual orientation, race, culture, gender, risk behaviour or socio-economic status – has the right to health and to the highest standard of affordable and accessible prevention, treatment and care, including preventive and therapeutic vaccines.

Social Justice. All members of society should be treated fairly, have their basic needs met, have access to the same services and have opportunities to participate in the creation of the response. All people living with HIV/AIDS and populations at risk should have equitable access to the best available therapies and interventions, including safe, effective HIV vaccines.

A Multifaceted Response to HIV. Vaccines are one part of a comprehensive response to HIV/AIDS and complement prevention and treatment efforts.

Participation and Empowerment. People living with HIV/AIDS and populations at risk are partners in planning, implementing and monitoring Canada's vaccine initiatives. Their diverse and unique rights and needs will drive all vaccine research.

A Multisectoral Approach. Canada will use a multisectoral approach that involves all levels of government, researchers, the community and the private sector to fulfil its role in HIV vaccines development and distribution and make full use of its expertise.

Strategic Coordination. Canada's HIV vaccines efforts will be based on collaboration among networks of researchers, policy makers, communities, the private sector, funders and other countries rather than competition. Canada will share its work with others and build on others' experiences, bringing together Canadian expertise for common goals.

Ethical Practice. All of Canada's vaccine efforts will be held to high ethical standards, including those set out in the *Ethical Considerations in HIV Preventive Vaccine Research – UNAIDS Guidance Document* developed by the World Health Organization (WHO) – and the Joint United Nations Programme on HIV/AIDS (UNAIDS).

Transparency and Accountability. Lives are at stake, and resources must be used wisely. Canada's vaccine initiatives are accountable to people living with HIV/AIDS and populations at risk for safety and efficacy, to all Canadians for their use of resources, and to the rest of the world for fulfilling their role in this global effort.

Long-Term Commitment. It will take many years to develop safe, effective vaccines. Canada is prepared to make the long-term sustained commitment required for successful vaccine programs.

¹ *Leading Together: Canada Takes Action on HIV/AIDS (2005-2010):*
www.leadingtogether.ca



What is the difference between a preventive and a therapeutic HIV vaccine?

A preventive vaccine is designed for individuals who are not infected with HIV. The vaccine would either prevent the individual from becoming infected when exposed to the virus, or if infection occurs, in the case of HIV, stop the disease from progressing as quickly to AIDS. A therapeutic vaccine would be designed to reduce the impact of HIV/AIDS in individuals already infected with the disease.

Source: International AIDS Vaccine Initiative



HIV vaccines must be positioned within a comprehensive response, linking prevention, testing, treatment and trials.

WHY DOES CANADA NEED AN HIV VACCINES PLAN?

There are two main reasons that Canada needs a vaccines plan:

1. The world needs preventive and therapeutic HIV vaccines that are safe, effective and globally accessible
2. Canada can make a difference – the plan will define how to enhance and coordinate Canada's role in the global efforts to find a vaccine

1. THE WORLD NEEDS HIV VACCINES

The epidemic continues to grow and kill

The global HIV/AIDS epidemic knows no borders.

According to UNAIDS,² in 2005:

- ⌘ 40.3 million people were estimated to be living with HIV
- ⌘ 4.9 million more people were newly infected with HIV -- the greatest number in any year since the beginning of the epidemic
- ⌘ 3.1 million people died of AIDS: 2.6 million were adults, and 570,000 were children under the age of 15.

Over 95% of HIV infections are occurring in poor and/or developing countries. Sub-Saharan Africa has just over 10% of the world's population but is home to more than 60% of all people living with HIV/AIDS.³ The virus is also spreading rapidly in other parts of the world, including the Caribbean, Eastern Europe, India, China, and Central and Southeast Asia.⁴ High rates of HIV infection in many developing countries are eroding recent gains in education, health care, security, environmental sustainability and political stability.

Even in a resource-rich country like Canada, the number of people living with HIV/AIDS continues to grow. By the end of 2002, about 56,000⁵ people in Canada were living with HIV, a 12% increase from 1999 estimates. In 2002, an estimated 2,800 to 5,200 people in Canada became infected.

Despite significant progress in HIV treatments, the virus continues to kill. Since the first cases of AIDS were identified in 1981, over 25 million people worldwide have died of AIDS-related illnesses – 3 million in 2003 alone. AIDS is now the leading cause of death in sub-Saharan Africa and the fourth-biggest global killer.⁶ As of December 31, 2004, a total of 13,111 AIDS-related deaths had been reported in Canada.⁷

Existing prevention strategies are not enough to stop AIDS

Prevention strategies are an essential part of an effective response to HIV/AIDS. They have helped slow the spread of HIV in many parts of the world. But existing prevention strategies will not be enough to stop AIDS.

Globally, half the people infected with HIV are women (in sub-Saharan Africa, 58% of people living with HIV/AIDS are women). Because of financial dependence, social customs and power imbalances within relationships – as well as the lack of prevention technologies controlled by women, such as microbicides – many women are unable to protect themselves (e.g., negotiate safer sex or drug use with their partners). ⌘⌘

In Canada, rates of HIV infection are particularly high in marginalized populations, such as gay men, people who use injection drugs, Aboriginal people, people from countries where HIV is endemic, vulnerable women, sex workers, and people in correctional facilities. People who suffer stigma and discrimination or who are poor, homeless or living with an addiction are also more vulnerable to infection and less able to protect themselves from HIV infection.

² UNAIDS/WHO AIDS Epidemic Update: December 2005

³ *ibid.*

⁴ *ibid.*

⁵ Public Health Agency of Canada. HIV/AIDS Epi Updates, May 2005.

⁶ UNAIDS. 2004 Report on the global AIDS epidemic.

⁷ Public Health Agency of Canada. HIV and AIDS in Canada. Surveillance Report to December 31, 2004.

Existing treatments are not enough to stop AIDS

Treatments are also an essential part of an effective response to HIV/AIDS. In countries where people have equitable, affordable access to highly active antiretroviral therapies (HAART), people with HIV are living longer, and the number of AIDS-related deaths has dropped. But there are limits to these treatments. Despite global efforts to improve access to antiretroviral therapy, including calls for universal access by 2010, these treatments will remain outside the reach of many who need them⁸, particularly people in those developing countries that have been hit hardest by HIV/AIDS. Antiretroviral treatments are expensive, have numerous side effects and have to be taken indefinitely, and their long-term efficacy is uncertain.

While the treatments may delay death, they are not a cure. More therapeutic options are desperately needed for people living with HIV/AIDS, including therapeutic HIV vaccines that may boost immune system function, delay disease progression and the need for treatment, and allow people to live longer, healthier lives.

Vaccines are one of the most powerful health interventions

Vaccines save millions of lives each year and have played a crucial role in controlling and, in some cases, eradicating infectious diseases. For example, consistent global vaccine/immunization programs have eradicated smallpox and significantly reduced diphtheria, polio and measles (see figure 1-33).

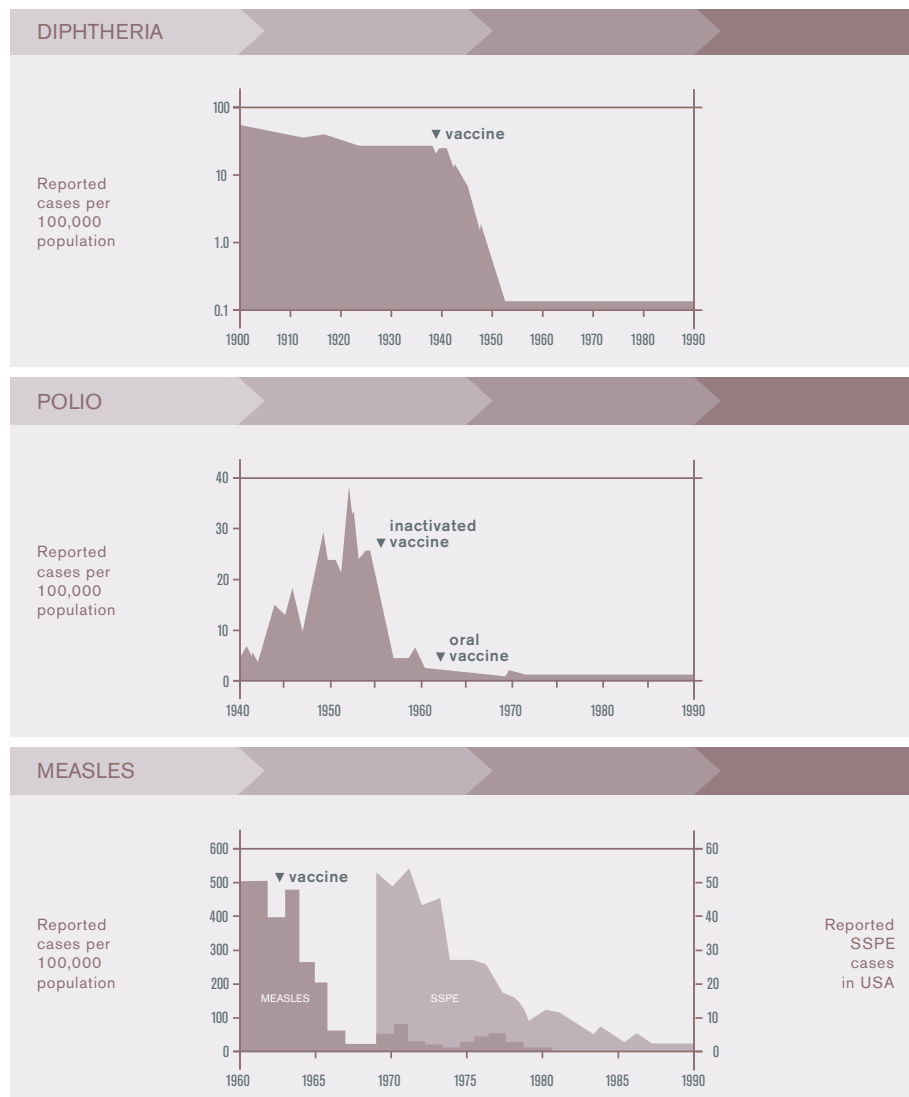


Figure 1-33 Immunobiology, 6/e.
(©Garland Science 2005)
Janeway, Traver, Walport & Shlomchik

⁸ At the end of 2005, only about 1 million people, out of the 6 million who need it, had access to antiretroviral therapies (WHO, 2005).

Most vaccines are “preventive,” that is, they are designed to protect people who are not yet infected and keep them from getting a disease. Preventive vaccines do not provide a cure or treatment for people who are already infected. “Therapeutic” vaccines are designed to treat people who are already infected. Researchers are currently working to develop therapeutic vaccines for HIV/AIDS as well as for a number of other conditions, including cancer, hepatitis C and addictions.

Calls for public health responses to emergencies such as SARS and avian influenza illustrate the public support and urgent need for capacity-building for vaccines.⁹ Canada’s National Immunization Strategy¹⁰ indicates that provincial and federal governments recognize that vaccines are important and a shared responsibility across all health sectors. Vaccines – along with treatments and other prevention techniques – form a mutually reinforcing control and management strategy for infectious diseases. They are a cost-effective part of the prevention-treatment-care continuum and should be part of a comprehensive response to HIV/AIDS.¹¹

Vaccine work is under way worldwide, and progress is being made

Advances in molecular biology and basic HIV research have identified promising strategies for effective HIV vaccines. Experimental vaccines have been used to protect non-human primates from infection by a virus closely related to HIV. The fact that people live an average of 10 years with HIV infection before developing AIDS means that the immune system already has some ability to fight the disease, and a vaccine could work to boost these natural defences. Some people repeatedly exposed to HIV resist infection. Their immune response may provide important clues to effective preventive and therapeutic HIV/AIDS vaccines.

Since 2000, the number of AIDS vaccine candidates in small-scale trials has doubled. According to IAVI, as of December 2004, 34 vaccine candidates were under development, and a number have been shown to be safe in small-scale clinical trials and to trigger HIV-specific immune response. The first large-scale trials were completed in 2003. Although the vaccine candidate did not prove effective, the trials demonstrated that it is possible to recruit thousands of volunteers and retain them over the three years required to assess a vaccine: this is key to ongoing vaccine research.

More and more countries – including a growing number of developing countries – are participating in vaccine research and development. As more countries become involved and the number of vaccine candidates and trials increases, it is vital that each country understand global efforts and have a plan to guide its contribution to what is truly a global initiative. Each country must also locate its efforts in the context of the Global HIV/AIDS Vaccine Enterprise,¹² which was initiated in June 2003 by an international group of scientists. The Enterprise describes the major roadblocks in HIV vaccine development, summarizes current scientific priorities, and describes an initial strategic approach to address those priorities, with the aim of stimulating both researchers and funders to explore new, more collaborative, cooperative and transparent approaches to addressing the major obstacles in HIV vaccine development. The Enterprise proposes to coordinate efforts at a global level, facilitate use of common tools and technologies and help ensure access to optimized resources. In June 2004, the Group of Eight (G8) countries endorsed the Global HIV Vaccine Enterprise. The Enterprise will take a number of steps to coordinate research and vaccine development, including developing a strategic plan, establishing a network of coordinated vaccine development centres, increasing vaccine manufacturing capacity, establishing standard protocols and measures of effectiveness for all vaccine trials so data can be shared, developing an international clinical trials system, addressing regulatory issues and encouraging greater involvement of scientists in developing countries. IAVI and the National Institutes of Health (NIH) in the United States have also formed the Neutralizing Antibody Consortium to speed progress in designing immunogens that elicit broadly neutralizing antibodies against HIV. This type of international collaboration will help ensure more coordinated, efficient use of research resources.

⁹ *Learning from SARS - Renewal of Public Health in Canada - A report of the National Advisory Committee on SARS and Public Health*. October 2003. <http://www.phac-aspc.gc.ca/publicat/sars-sras/naylor/>

¹⁰ *Final Report: National Immunization Strategy - A Report from the F/P/T Advisory Committee on Population Health and Health Security (ACPHHS) to the Conference of F/P/T Deputy Ministers of Health*. http://www.phac-aspc.gc.ca/publicat/nat_immunization_03/

¹¹ *Joint Advocacy on HIV/AIDS Treatment, Microbicides and Vaccines. Statement of Commitment to Building a Comprehensive Global HIV/AIDS Response*. November 2003. <http://www.aidslaw.ca/Maincontent/issues/vaccines/MTV/MTVStatofC.pdf>

¹² *Coordinating Committee of the Global HIV/AIDS Vaccine Enterprise (2005). The Global HIV/AIDS Vaccine Enterprise: Scientific Strategic Plan*. *PLoS Med* 2(2): e25.

2. CANADA CAN MAKE A DIFFERENCE

Because developing HIV vaccines is a global effort, Canada must be involved. We can make a difference. Canada should pursue the continuum of activities involved in the development of HIV vaccines as a coordinated effort, partnering with other countries, integrating lessons learned globally into the Canadian experience and ensuring that expertise developed in other countries is applied in Canada.

Effective International Collaboration. Canadian researchers also have more than 20 years' experience and strong working relationships in developing countries in Africa and other parts of the world. Many of these researchers have demonstrated a commitment to working internationally and are willing to continue contributing. More specifically, Canada has contributed to capacity building for developing countries with respect to clinical trials and has developed the Global Health Research Initiative,¹³ which aims to shape and respond to the global health research agenda, influence policy and policy coherence relating to global health research and facilitate information sharing among partner agencies. The Canadian government has already demonstrated its leadership and commitment to developing new prevention technologies for HIV/AIDS by providing funding for international vaccine and microbicide initiatives. Support for international research efforts must continue, and support for domestic research efforts must be enhanced.

Research Capacity. Canada has extensive scientific expertise in vaccine development, particularly in the areas of recombinant vaccine delivery systems, mucosal immunity and immune monitoring, and social and behavioural science. This can help guide vaccine policy and delivery programs. Canada also has a strong health research capacity that makes it possible to respond quickly to health challenges. It took Canadian researchers only 11 weeks, for example, to map out the genetic sequence of the coronavirus associated with SARS.

Research Infrastructure. Canada has a strong scientific infrastructure to support vaccine research and the potential to contribute clinical research sites to local and international trials. In 2004, the Canadian Foundation for Innovation (CFI), through its International Access Fund, provided \$3.8 million to an international team led by the University of Manitoba¹⁴ for the construction, refitting and equipping of state-of-the-art laboratories that focus on retrovirology, hemorrhagic fever virology, functional immunology and emerging pathogens. Facilities for imaging, flow cytometry, molecular biology (including DNA preparation), serology, genomics and bioinformatics will also be established. Through its Research Hospital Fund, in 2004 the CFI also contributed \$5 million to the Centre hospitalier de l'Université de Montréal for an Integrated Research Centre in Human Immunology, Immunotherapy and Vaccinology. With this support and with future investments, Canada is well placed to support vaccine research, development and production.

Clinical Trial Infrastructure. The Canadian HIV Trials Network (CTN) is an effective network that has experience conducting vaccine trials in Canada. It can play a major role in conducting the trials, overseeing all the regulatory aspects of coordinating and implementing the clinical trials, conducting data analysis and reporting the results. Canadian investigators have more than 20 years' experience working on HIV/AIDS in Kenya, and the Canadian Network for Vaccines and Immunotherapeutics (CANVAC) has established collaborations with investigators in Africa (e.g., the Kenya AIDS Vaccine Initiative). A CFI-funded laboratory has been built and can provide on-site real-time immune and virological assessments for vaccine trials.

private-public sector partnerships. Various partners have explored ways to collaborate in the Global HIV/AIDS Vaccine Enterprise, and some private-public sector partnerships are being explored. There have been partnership discussions initiated between researchers and sanofi pasteur (a pharmaceutical company devoted to vaccines research) regarding the development of a production plant for HIV vaccines.

¹³ *The Global Health Research Initiative is an agreement of cooperation between CIHR, CIDA, Health Canada and the International Development Research Centre aimed at coordinating and building upon Canada's global health research activities.*

<http://www.cibr-irsc.gc.ca/el/7350.html>

¹⁴ <http://www.innovation.ca/medial/index.cfm?websiteid=316>

Strong Community. We have strong, organized and informed communities of people living with or at risk of HIV/AIDS who could play a key part in shaping vaccine research, policies and programs. Community-based organizations are key players in efforts to recruit trial participants while ensuring that prevention messages are maintained and delivered in creative, culturally appropriate ways. Canada's community-based organizations can provide models of non-government organization (NGO) structure and governance and models of formalized engagement of communities in advocacy with respect to HIV vaccine trials.

Multisectoral Collaboration. Canada has a multi-stakeholder plan – *Leading Together: Canada Takes Action on HIV/AIDS (2005-2010)* – and a well-established collaborative model of government working with the community to address HIV/AIDS issues. A collaborative initiative with respect to vaccines research, including HIV vaccines, CANVAC was established in 2000 and operated until March 2006. This unique network comprised 75 of the most highly recognized Canadian research teams specializing in the fields of immunology, virology, molecular biology and social sciences and affiliated with 21 Canadian universities and research institutes across the country. CANVAC collaborated with corporate partners and interested government agencies and community groups to develop safe, effective vaccines and immunotherapies to prevent and treat diseases related to HIV, hepatitis C virus and cancer. Canada needs a continuation of collaborative efforts between the pharmaceutical industry and academic researchers, each of which is needed to push and balance the other in their important roles in HIV vaccines research and development.

HIV Legal, Ethical and Human Rights Issues. Canada has made commitments to protect and fulfil human rights and to achieve global health, and could provide a model for protecting the human rights of people who participate in vaccine trials. Canada has also contributed analysis of legal, ethical and human rights issues associated with HIV/AIDS and vaccines.¹⁵

Universal Health Care System. Canada's health care system is a group of socialized health insurance plans that provides coverage to all Canadian citizens. It is publicly funded and administered on a provincial or territorial basis within guidelines set by the federal government. Under the health care system, individual citizens are provided with preventive care and medical treatments from primary care physicians as well as access to hospitals, dental surgery and additional medical services. With a few exceptions, all citizens qualify for health coverage regardless of medical history, personal income or standard of living.

Immunization Experience. Canadian children in all provinces and territories are routinely immunized against nine diseases,¹⁶ and high-risk adults are also given free access to influenza vaccines. Thus, there is a culture of acceptance of vaccination in Canada that will help in advocacy for equal access to an HIV vaccine and a vaccine-delivery infrastructure across Canada. Canada also has extensive experience promoting existing adult vaccines (e.g., hepatitis A and B, influenza, pneumonia, meningitis) within vulnerable or marginalized communities, and we can use this experience to help cultivate community receptiveness to HIV vaccines.

Continuum Approach. Canada's approach to addressing its HIV/AIDS epidemic is to support and deliver a continuum of services from prevention to diagnosis, care, treatment and support. While some community-based organizations specialize in certain parts of the continuum, their services are always recognized as being complementary to a wider effort to address HIV/AIDS through an integrated approach.

Experience Conducting Trials and Engaging Communities. Canada already has a strong clinical trial infrastructure, an established regulatory system and considerable expertise in organizing, conducting and evaluating clinical trials: expertise that can be applied at home and abroad. For example, Canada managed three clinical test sites for one of the first two Phase III HIV vaccine trials run worldwide. Although the candidate did not prove to be effective, the Canadian sites were well run. The trial sites in Canada

¹⁵ Thompson D. *HIV Vaccines in Canada: Legal and Ethical Issues – A Backgrounder*. Canadian HIV/AIDS Legal Network. 2001

¹⁶ polio, pertussis, tetanus, diphtheria, *Haemophilus influenzae* type b, measles, mumps, rubella and hepatitis B.

also helped develop innovative ways of linking vaccine research with HIV prevention and addressed the long-standing concern that the vaccine development process would contribute to an increase in risk-taking behaviours.

Canada has the systems in place to ensure ethical recruitment. Community-based organizations have developed collaborative relationships with communities most affected by HIV – gay men, people who use injection drugs, Aboriginal people, people from countries where HIV is endemic, women, youth, people in correctional facilities – that help ensure they will be active participants in planning for and conducting trials. At the end of 2005, two therapeutic HIV vaccine trials were under way in Canada. Also, Canada has participated in two preventive HIV vaccine trials (Phases IIb and III). During the Phase III vaccine trial, the Canadian sites worked with people living with or at risk of HIV to set up community advisory boards (CABs) responsible for providing the link between the trial organizers and the affected community and helping researchers understand the target communities. The Canadian sites also advocated successfully for changes in the trial protocol to include women. In late 2004, a large Phase IIb trial established a site in Canada. Canadian community advocates became involved and helped the lead investigators understand Canadian expectations for community involvement and develop a CAB and an education plan. ¹⁷

The federal government has made a commitment

In response to advocacy from Canadian community-based organizations and researchers, in July 2002, at the International AIDS Conference in Barcelona, Spain, Dr. Paul Gully (then Senior Director General in Health Canada and now Deputy Chief Public Health Officer in the Public Health Agency of Canada), announced that Canada would develop an HIV vaccines plan. The Government acknowledged that to spark Canada's vaccine efforts at home and abroad we need a coordinated plan.

That commitment to HIV vaccines was reinforced in June 2004 when Canada joined the other leaders of the G8 industrialized countries in agreeing to fund a Global HIV Vaccine Enterprise – a consortium of government and private sector groups – to coordinate and accelerate HIV vaccine research. To be able to contribute effectively to the Global HIV Vaccine Enterprise, Canada needs its own coordinated HIV vaccines plan. For example, while Canada spends about \$1.3 million annually on HIV vaccine research, the United States allocates \$600 million (USD) and France 8 million (Euros).¹⁷

Leading Together: Canada Takes Action on HIV/AIDS (2005-2010) reiterates the need for Canada to be actively involved in vaccine development and delivery, to contribute to global efforts to develop vaccines and to ensure equitable access to vaccines as they become available. Canada also agreed to increase and accelerate research on HIV vaccines by endorsing the UNGASS Declaration of Commitment on HIV/AIDS. The UNGASS Declaration calls on governments to increase their investment in HIV vaccine research and development and identifies as one of its priorities “to redouble the search for a vaccine, as well as a cure.” ¹⁸

The Canadian HIV Vaccine Enterprise (CHIVE), proposed in 2005, aimed to fulfil Canada's commitment to the Global HIV/AIDS Vaccine Enterprise and to HIV vaccine development and global public health in general. CHIVE was the result of collaboration among several Canadian and international partners from academia, industry and government, all working to support the objective of the Global Enterprise. CHIVE partners included the members of the former CANVAC, the CTN, sanofi pasteur, the Bill and Melinda Gates Foundation and the International Consortium for Infectious Disease (ICID). Canadian collaborators in CHIVE included CIHR, CIDA, the International Development Research Centre (IDRC), Canada Science International (CSI) and SHI Consulting. This proposed public-private partnership would have added particular value to HIV vaccine development efforts through several attributes, such as the diversity of its associated organizations, its commitment to translational research, its roots in many regions of Canada and its access to development and manufacturing expertise and to specialized infrastructure



THE STAGES OF CLINICAL TRIALS

PHASE I: a clinical trial with a small number (usually 60 or fewer) of healthy volunteers, typically at low risk for HIV infection. Phase I trials test a vaccine's safety in humans, including its metabolic and pharmacologic actions and any side effects seen with increasing doses.

PHASE II: a controlled clinical study to identify common short-term side effects and risks associated with the test vaccine and to collect expanded information on its immunogenicity (its effects on the immune system). Phase II trials enrol some volunteers with characteristics similar to potential participants in an efficacy (Phase III) trial. They enrol up to several hundred participants and generally have two or more arms.

PHASE III: a large controlled study to determine the ability of a vaccine to produce a desired clinical effect on the risk of a given infection, disease or other clinical condition at an optimally selected dose and schedule. These trials also gather additional information about safety needed to evaluate the overall benefit-risk relationship of the vaccine. Phase III trials usually include several hundred to several thousand volunteers.

POST-APPROVAL SURVEILLANCE SYSTEM: Medications often come with toxicities that are not detected until after the drug is approved. The system for tracking adverse drug events after the drug goes to market is called a post-approval surveillance system, or PASS.



Canada committed to:

Encourage increased investment in HIV/AIDS-related research nationally, regionally and internationally, in particular for the development of sustainable and affordable prevention technologies, such as vaccines and microbicides, and encourage the proactive preparation of financial and logistic plans to facilitate rapid access to vaccines when they become available.

UNGASS Declaration of Commitment on HIV/AIDS (June 2001), paragraph 89.

¹⁷ *Standing Committee on Health, June 2003 and Center for HIV/AIDS Vaccine Immunology (CHAVI).*

necessary for the pre-clinical and clinical development of vaccines. When the funding for CANVAC was not renewed beyond 2006, this proposed initiative was discontinued.

Although the Canadian government has made a number of commitments relating to HIV/AIDS and research – UNGASS Declaration of Commitment on HIV/AIDS, *Leading Together: Canada Takes Action on HIV/AIDS (2005-2010)*, the Federal Initiative to Address HIV/AIDS in Canada, the G8 Gleneagles Africa Statement, Dr. Paul Gully's commitment at the 2002 International AIDS Conference, CIDA's Canada Fund for Africa, human rights commitments, the Standing Committee on Health, CIHR's HIV/AIDS Research Advisory Committee's priority for new prevention technologies – none have been specifically targeted to HIV vaccines research in Canada.

A Canadian HIV Vaccines Plan will help fulfil our human rights obligations and protect the rights of people who participate in Canadian vaccine trials

Health and human rights are inextricably linked. Enjoying the highest attainable standard of health is a human right. Fulfilling this and other human rights will reduce vulnerability to HIV and its impact.¹⁸ Under international covenants and treaties on human rights to which Canada is a signatory,¹⁹ governments are obliged to respect, protect and fulfil the right to health for HIV-positive people and provide access to the best possible prevention technologies for people who are HIV-negative.²⁰ Because effective vaccines will be one means by which to help ensure people's right to health, Canada should support vaccine development as one method of fulfilling its commitment to human rights.²¹

Human rights law guarantees people the right to not be subjected to scientific studies or experimentation without their consent. Fully informed consent and confidentiality are essential in all research involving humans. People who participate in clinical trials also have the right to full information about all aspects of the research, the right to redress and treatment if injured during a study and the right not to be tested for HIV without consent and counselling. A comprehensive HIV vaccines plan will help to ensure that the rights of trial participants are protected, that barriers to the participation of marginalized people are removed to the extent possible, and that there is meaningful participation in decision making about how and with whom clinical trials are conducted.

A Canadian HIV Vaccines Plan will increase opportunities to engage the private sector

To meaningfully contribute to the global efforts to develop HIV vaccines, Canada needs greater involvement of the private sector in vaccine research and development. New drug development is usually funded by the major pharmaceutical companies, who are able to pay for large clinical trials and other costly research processes. The private sector will not participate unless there are economic incentives. Pharmaceutical companies may be reluctant to engage in HIV vaccines research for a variety of reasons, including liability concerns, lack of in-house expertise and an uncertain regulatory environment. Their main concern, however, is that the new products may not be profitable enough to justify the cost of developing them. Pharmaceutical companies are driven by economic self-interest, so they are not motivated to invest in a product just because it is needed. There are many products – like malaria vaccines, new contraceptives, or microbicides – that would yield huge returns to society in terms of productivity and health benefits but that hold little profit potential for private investors. Such products are known collectively as "public health goods," and they are developed only if government and foundations invest the funds needed to do so.

A combination of carefully designed, adequately funded and politically backed measures – both pushing and pulling – could have a significant effect on the level of research and development (R&D) spending for HIV vaccines, on the quality and effectiveness of this research and product development effort and ultimately on the speed with which an efficacious vaccine for all regions is produced and made accessible to those who need it. To be effective, the mix of push and pull measures should stimulate not only the large bio-

¹⁸ *Joint Advocacy on HIV/AIDS Treatments, Microbicides and Vaccines. Statement of Commitment to Building a Comprehensive Global HIV/AIDS Response.* November 2003.

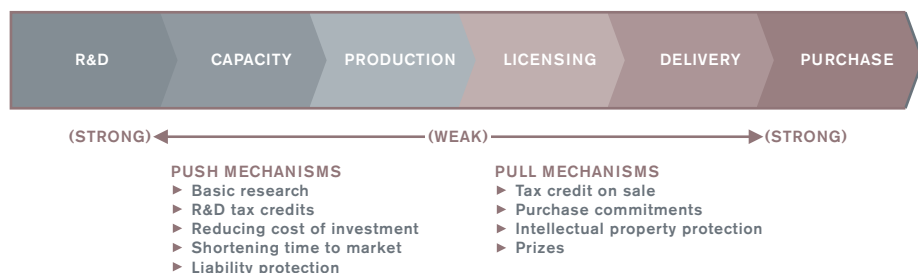
<http://www.aidslaw.ca/Maincontent/issues/vaccines/MTV/MTVStatofC.pdf>

¹⁹ *Including the Universal Declaration of Human Rights; various resolutions adopted by the United Nations Commission on Human Rights; the Convention on the Rights of the Child; the Vienna Declaration and Programme of Action; the World Conference on Human Rights, June 1993; the International Guidelines on HIV/AIDS and Human Rights; and Ethical considerations in HIV preventive vaccine research – UNAIDS guidance document.*

²⁰ *Thompson D. HIV Vaccines in Canada: Legal and Ethical Issues – A Background.* Canadian HIV/AIDS Legal Network. 2001.

²¹ *Ibid.*

pharmaceutical companies but also the smaller biotechnology companies that have been an important source of technical innovation in recent years. Push mechanisms reduce the cost of R&D and to a lesser degree the cost of manufacturing a vaccine. They focus on giving industry added incentives to invest in R&D inputs, generally by subsidizing the cost of these inputs. If these subsidies are targeted to high-quality scientific research and product development, they can prove to be highly effective. It is inherently difficult for governments to pick “winners” in R&D, however, so there is always the risk of financial investment without a successful outcome in terms of product development. Possible push and pull mechanisms are summarized in the figure below.²²



Having a Canadian HIV Vaccines Plan will help Canada elaborate on and explore economic incentives and private-public sector partnerships, explore ways to leverage corporate social responsibility, and encourage good corporate citizenship among private partners. A plan will bring together different government departments, such as the Public Health Agency of Canada, Health Canada, Canada Revenue Agency, Foreign Affairs Canada and Industry Canada, to make the business and economic case for investing in HIV vaccines research and to identify government programs that could be used to provide economic incentives (i.e., push and pull mechanisms) that will encourage the private drug industry to invest in HIV vaccines research. ❷



IAVI anticipates that a comprehensive package of push and pull inducements would cost governments and taxpayers billions of dollars in tax relief and guaranteed purchase funding. But the economic and social “returns” on an AIDS vaccine are so large that they dwarf the costs involved – UNAIDS estimates that \$20 billion will be needed for prevention and care in low- and middle-income countries by 2007. Bold and imaginative steps need to be taken by world leaders today to create strong incentives for industry to invest in finding a vaccine that prevents the spread of AIDS.

International AIDS Vaccine Initiative: Policy Brief - Incentives for Private Sector Development of an AIDS Vaccine Policy Brief #2/September 2004

²² *International AIDS Vaccine Initiative: Policy Brief - Incentives for Private Sector Development of an AIDS Vaccine. Policy Brief #2/September 2004*

ELEMENTS OF A CANADIAN HIV VACCINES PLAN

COMPONENTS/STRATEGIES

15

The Canadian HIV Vaccines Plan identifies a range of different strategies designed to address the six key components of effective HIV vaccine development:

1. DISCOVERY:

Take an integrated strategic approach to HIV vaccine research and development

2. TRIALS AND TESTING:

Enhance Canada's capacity to conduct vaccine trials

3. PRODUCTION:

Develop Canada's capacity to manufacture vaccines

4. DISTRIBUTION:

Ensure equitable access to HIV vaccines at home and abroad

5. COMMUNITY ENGAGEMENT:

Engage Canadians in vaccines research, production and distribution

**6. POLITICAL LEADERSHIP AND
FINANCIAL COMMITMENT:**

Provide long-term, dedicated leadership and funding.

The components of the vaccines plan are presented in six sections, but it is important to note that the components are not arranged in a temporal progression. Rather, some of the components must happen simultaneously, as depicted in Appendix A.

The following sections set out the challenges and issues associated with each component, as well as the strategies that should be developed and implemented in a Canadian plan.

1.

DISCOVERY

TAKE AN INTEGRATED STRATEGIC APPROACH TO HIV VACCINE RESEARCH AND DEVELOPMENT

17

THE CHALLENGES

As the world works to discover HIV vaccines, it faces some key challenges, including gaps in current research programs, the need for more coordinated research efforts and the need to attract and retain scientists and researchers.

Research gaps. Despite the progress that has been made, after more than a decade of HIV vaccine research some fundamental scientific questions remain unanswered. For example, scientists do not know which HIV antigens and immune responses will give people protective immunity or how to trigger neutralizing antibodies that will be effective over the long term. They do not yet know which vaccine designs will be most effective in stimulating mucosal immunity, how to design vaccines that will fight the different strains of HIV (nine have been identified to date in different geographic regions), or which vaccine designs will provide the same protection as live-virus vaccines but with fewer risks.

These gaps in scientific knowledge reflect a gap in research. Current vaccine development efforts have tended to focus either on basic research (i.e., HIV virology, immunology, molecular biology, pathogenesis, animal models) or product development (i.e., vaccine candidates and mechanisms to evaluate them). Almost all the vaccine candidates now in trials are similar: they are all trying to elicit a cell-mediated immune response. If the hypothesis that a vaccine can confer protection through a cell-mediated immune response is incorrect, the current candidates will be irrelevant.

Missing are innovative research and vaccine design – the thinking and studies that will solve these critical problems – as well as an interest in testing other hypotheses, such as a broadly neutralizing antibody immune response, a mucosal immune response, or mechanisms to achieve the same effect as live-attenuated vaccine. Many researchers are convinced that the most effective HIV vaccines will need to induce both cellular and antibody-based immunity.²³ This type of research will require the multidisciplinary involvement of scientists in a number of fields, creative approaches and long-term commitment. Many of the world's most significant scientific discoveries (e.g., the discovery of penicillin) were accidents recognized as advancements only because the scientists had open minds and basic scientific curiosity. The Canadian HIV Vaccines Plan should not be interpreted as a prescriptive plan for the ways in which to conduct HIV vaccine research.

²³ IAVI Report 6(3) May-June 2002.



TYPES OF IMMUNE RESPONSES

INNATE IMMUNITY: An evolutionary ancient defence against infection that exists prior to and is ready for immediate activation following infection. It consists of anatomical/physical barriers (e.g., intact skin and mucosal barriers), chemical barriers (e.g., acidity of stomach, antimicrobial factors), innate cells (e.g., phagocytic cells, natural killer [NK] cells) and inflammatory responses. Innate immune responses are triggered by receptors on cells, such as toll-like receptors (TLRs), which detect molecules on pathogens that are generally absent from the host.

ANTIBODY-BASED OR HUMORAL IMMUNITY: Host defences carried out by antibodies, also called immunoglobulins, in blood plasma, lymph and tissue fluids. Antibodies are produced by a type of white blood cell called B-cells that express a specific antibody or immunoglobulin on their cell surface as their antigen receptor. Antibodies primarily protect against infectious agents and their products (e.g., toxins) that are found outside cells in the body. Antibodies bind to and neutralize pathogens or prepare them for uptake and destruction by phagocytic cells. Transfer of antibodies confers this type of immunity on recipients.

CELLULAR IMMUNITY: Host defences that are carried out by antigen-specific T-cells. Cellular immunity protects against intracellular bacteria, viruses and cancer cells and is responsible for graft rejection. Transfer of immune T-cells confers protection on the recipient.

ADAPTIVE IMMUNITY: Host defences carried out by antigen-specific B-cells and T-cells following infection or immunization, hence adaptive immunity is both humoral and cellular immunity. Adaptive immune responses usually take some time (days to weeks) to develop because the specific immune cells must first expand before they develop into effector cells that can remove the pathogen. Adaptive immune responses are highly specific and exhibit memory immune responses.

MUCOSAL IMMUNITY: Most infectious agents enter the body and initiate infection through the mucosal membranes that line the respiratory, digestive and urogenital tracts. Mucosal surfaces are defended by a mucosal immune system that consists of immune cells and antibodies, including secretory IgA antibodies, present in the lining that covers the mucosal surfaces and in the underlying layers.

Canada is in a strong position to help fill some of these gaps. Essential for discovery is collaboration across disciplines and research teams. CANVAC was one example of multidisciplinary investigators coming together to develop preventive and therapeutic HIV vaccines (as well as vaccines for cancer and hepatitis C).

Need for more coordinated, collaborative action. Global efforts to develop HIV vaccines have been fragmented and duplicative. There has been no consistent approach or common criteria for deciding which products should progress through trials and no mechanism to compare similar products to assess which ones are most promising and should be given priority. There has been little collaboration among researchers and no mechanisms to coordinate research activities or establish priorities. This is changing.

Individual countries, including Canada, are working to integrate their vaccine efforts with global initiatives. Canada is exploring models of collaboration between the pharmaceutical industry, researchers, government and community-based organizations, building on lessons learned from CANVAC. ✕

Need for more vaccine scientists and researchers and more commitment to vaccine research. Vaccine research is currently conducted by a handful of scientists and researchers worldwide. Because vaccines have relatively small profit margins, there is little incentive for the private sector to invest in developing vaccines. In most cases, the task is left to public health and academic researchers who must rely on government funding for their research programs.

Worldwide, more effort must be made to develop and nurture vaccine scientists. This is also true in Canada, where only a handful of researchers are involved in vaccine research. In addition, there is a serious gap in private sector involvement in HIV vaccine research. Between 1996 and 2002, the amount that private drug companies invested in HIV research declined. Currently, only 15% of the funding for HIV vaccine research comes from the drug industry, while 85% comes from governments and foundations. The reason for this gap is largely economic: it is more attractive for companies to develop multiple-dose life-long therapies than preventive medicines and interventions.

THE STRATEGY

To ensure that it makes a significant contribution to HIV vaccine discovery, Canada should:

1.1

Develop a Canadian HIV vaccine discovery agenda that builds on Canada's strengths and is located in the context of the international research agenda. Bring together the organizations that fund vaccine research (e.g., CIHR, Health Canada, Public Health Agency of Canada, CIDA), researchers (e.g., Canadian Association for HIV Research, CTN, CANVAC members) and the community (e.g., CAS, Canadian Treatment Action Council), and consult with international partners.

1.2

Establish a strong, well-resourced, strategic, coordinated Canadian vaccines discovery mechanism.

1.3

Build as quickly as possible the critical mass needed for discovery efforts with respect to researchers, products, funding and infrastructure. For example, enhancing access to CIHR Personnel Training Awards and Investigator Salary Awards (and other research funding bodies) could contribute to capacity building. Explore the development of HIV-vaccine-focussed strategic training initiatives in health research to enhance the capacity of networks and to train new investigators in basic, clinical and applied research. Build capacity in vaccine research.

1.4

Encourage researchers and industry to collaborate in translational research that helps to establish appropriate infrastructure so that viable candidates or concepts are brought into a streamlined, pre-clinical process. Translational research would generate data, clinical materials and clinical infrastructure (e.g., epidemiological laboratories, trials infrastructure) during the pre-clinical development of the vaccine that will be needed in clinical research.

2. TRIALS AND TESTING

ENHANCE CANADA'S CAPACITY TO CONDUCT VACCINE TRIALS

THE CHALLENGES

Vaccine candidates have to be tested, first in small-scale and then in large-scale clinical trials.

At present, the ability to move candidates into trials is limited by the lack of global capacity to conduct trials and by the logistical challenges of recruiting participants, particularly when trials of one vaccine may be run in different countries and in different population groups. As the number of vaccine candidates increases, these problems will be exacerbated.

Capacity to conduct trials. The world has little capacity to conduct large-scale trials – particularly in Africa or Asia where the epidemic is having the greatest impact. These countries have few sites able to manage trials, and many lack the regulatory expertise and infrastructure to review and approve trials in a timely way. In all of sub-Saharan Africa, there are only two immunology laboratories outside South Africa that meet the international quality assurance standards required for AIDS vaccine trials.²⁴ ❧

Canada's previous trial experiences can and should be used to identify opportunities to strengthen our capacity to participate in future trials, including Phase IIb or intermediate-sized trials that can be done more quickly than traditional Phase III trials to assess the potential efficacy of a vaccine. This approach allows more innovation, but care must be taken to ensure proper trial design and to understand its limitations.

Any vaccine candidates developed by Canadian researchers will also have to be tested for efficacy in trials in other countries.

Capacity to recruit participants.²⁵ Researchers estimate that 50,000 to 100,000 trial volunteers will be needed over the next five to 10 years, yet even experienced investigators in well-established clinical trial programs in the U.S. are concerned about their capacity to recruit. They question whether traditional recruitment strategies will supply enough volunteers. Few trial sites have the HIV prevalence and incidence data on potential volunteers required to plan and conduct large-scale trials. There has even been difficulty recruiting HIV vaccine trial participants among gay men, a group that traditionally has been very engaged in HIV/AIDS research efforts. Recruiting among other populations at risk has posed significant challenges as well.



Phase I trials would be done in Canada if the candidate product was developed in Canada.

Because Canada does not have a high incidence rate, it is unlikely to be a primary site for Phase II or Phase III clinical trials. Any trials conducted in Canada will likely be arms of larger trials conducted in other countries, and the role of Canadian clinicians and researchers will be to recruit participants and manage the trial sites (i.e., administer vaccine, monitor participants, submit data).

²⁴ 2005 AVAC Report, *AIDS Vaccines at the Crossroads*.

<http://www.avac.org/reports.htm>

²⁵ *Ibid.*

Canada is in a much stronger position than many countries to conduct clinical trials, but we will need to expand significantly our clinical research infrastructure and our ability to recruit participants to support a number of concurrent vaccine trials. In order to be ready for future clinical trials, proactive development and maintenance of trial registries and “readiness cohorts” should be led by the Canadian HIV Trials Network (CTN).²⁶ It is important that previous cohorts of trial participants are not lost but rather built upon in order to test vaccine readiness as well as vaccine efficacy. Because recruiting participants for vaccine trials in Canada is proving difficult, Canada should also work to establish trial infrastructures internationally.

While Canada has an effective regulatory system for approving vaccines for testing, it has not fully addressed the issue of liability for any harm that results from participating in a trial. We must also ensure that we have the infrastructure in place to provide ongoing care and treatment for people who participate in clinical trials.

Representativeness of trial participants. HIV vaccine trials must include adequate representation of affected populations relative to the trial setting. In Canada, where there are fundamental disparities in access to trial participation – based on factors such as gender, age, rural setting, ethnocultural minorities, etc. – efforts must be made to ensure equitable representation of certain vulnerable and marginalized populations. We have to ensure that trials include populations that are epidemiologically relevant with respect to HIV prevalence and incidence and populations that are most likely to receive the vaccine (or would benefit even from a low-efficacy vaccine). Representativeness of trial participants will depend on trial design factors, such as whether the vaccine being tested is therapeutic or preventive, Phase II or Phase III, international or domestic. 

From a human rights perspective vis-à-vis the right to benefit from medical advancements, vulnerable populations must be given the opportunity to participate in vaccine trials; at the same time, they must not be expected to bear an undue burden of research. All vaccine trials must simultaneously develop a concrete plan for access in developing countries should the trial vaccine prove efficacious enough for distribution. Research must be inclusive of both sexes and of adolescents. People who use injection drugs have not yet been included in HIV vaccine trials, but they are a key population that would likely most benefit from an HIV vaccine, even if it is only partially efficacious. They would likely experience a different immune response than other candidates, and trials should explore different dosages or booster shots. Part of Canada’s contribution may be in laying the groundwork for reducing the stigma and discrimination of living with HIV, a necessary precondition of rolling out vaccine trials, especially in Aboriginal communities.



CANADA COMMITTED TO:

By 2003, ensure that all research protocols for the investigation of HIV-related treatment, including anti-retroviral therapies and vaccines, based on international guidelines and best practices, are evaluated by independent committees of ethics, in which persons living with HIV/AIDS and caregivers for anti-retroviral therapy participate.

UNGASS Declaration of Commitment on HIV/AIDS (June 2001), paragraph 74.

Capacity to address ethical issues. Canadian researchers have an ethical responsibility to their communities to conduct HIV vaccine trials in Canada to ensure that our populations living with or vulnerable to HIV are represented in global vaccine trials and to make sure that trial results are generalizable to our own populations at risk of HIV. Furthermore, researchers have an ethical responsibility to communicate with participants after the conclusion of clinical trials to share information about the results of the research and the implications.

In the past, people recruited to participate in research – particularly those from marginalized communities – often participated without giving their consent or without fully understanding the potential implications. This makes it more difficult to recruit people from marginalized communities in Canada, who may be suspicious of trials and fearful that their rights may be violated. This problem may be exacerbated when the trials involve countries that have not yet established standards and rules for ethical recruitment or endorsed established international standards. Because there are risks involved, it is critical to develop policies and supports that acknowledge and respect participants’ rights (e.g., compensation for any vaccine-related injury, and/or the best available care for people who become infected while participating in a trial).

Based on experience to date, people willing to participate in trials of HIV preventive vaccines are often highly vulnerable: they are more likely to be younger, unemployed, to live in unsta-

²⁶ *The CTN’s Core Group on Vaccines and Immunotherapies has a working group called the “Observational Study Working Group.”*

ble housing, to have practised unsafe sex or drug use, and to have low self-esteem. This means that the ethical standards for trials involving these participants have to be high. Participants in clinical trials should be informed about the potential benefits and risks and be recruited in a way that is legal, ethical and meets international research and human rights standards. Recruitment will be particularly difficult for trials of preventive vaccines where it may take many years of testing before a trial yields significant results. The selection of trial participants should also take into account the impact of participation on the individual, ensuring that individuals' participation in HIV vaccines trials is confidential and does not result in their experiencing discrimination or other abuses of their human rights. An ethical approach to recruitment from the beginning will make it easier to recruit people for future trials.²⁷ In addition to selecting participants carefully, all clinical trials should comply with UNAIDS guidelines.²⁸

THE STRATEGY

To enhance our capacity to conduct clinical trials and ensure that people living with HIV/AIDS and populations at risk in Canada have the opportunity to participate in ethical, well-run trials that benefit their communities, a Canadian HIV vaccines plan would:

2.1

Enhance the infrastructure (e.g., cohorts of participants, immune monitoring, standardization of assays) required to support clinical trials in Canada and internationally (i.e., wherever Canadian researchers are working or where Canada supports trials). Address any policy barriers to conducting clinical trials (e.g., regulatory, liability concerns for vaccine-related harms) and the strategies to overcome them (e.g., policy changes). Establish and support vaccine trial centres in Canada that would be responsible for coordinating all trials in their region, maintaining a registry of trial participants, doing post-trial follow-up and communication, and conducting long-term tracking studies and safety evaluations.

2.2

Develop a coordinated effort to partner with other countries to build centres of HIV vaccines trials, focussing primarily on trial implementation and monitoring. Integrate lessons learned globally into the Canadian experience, ensuring that clinical trials expertise developed in other countries is applied in Canada. Identify ways to share Canadian expertise in clinical trials in developing countries.

2.3

Ensure that all affected populations in Canada are given the opportunity to participate and that trials reflect communities that need vaccines the most. Identify effective community-specific recruitment and retention strategies, such as using surveillance data (e.g., prevalence, incidence, strain data) to identify and establish a roster of people willing to participate in trials when an appropriate vaccine candidate becomes available.

2.4

Develop a communications strategy that will ensure target populations participate in the design and implementation of vaccine trials; establish community advisory boards (CABs) or other mechanisms for each trial site and provide training for community participants; identify the communities' expectations/needs for and rights to information and support (e.g., insurance, compensation); define how information will move from researchers to the community and who is responsible for disseminating information; establish protocols for community involvement/education for all HIV vaccine trials conducted in Canada (e.g., methods to ensure informed consent); and identify the resources required to support effective community engagement and communication.

2.5

Ensure that clinical trials conduct is consistent with national and international ethical guidelines (e.g., UNAIDS Guidelines²⁷ and Tri-Council Guidelines) and monitor how well research projects are conforming to the ethical guidelines.²⁸

²⁷ HIV InSite. *Ethical Dimensions of HIV/AIDS: Special Issues in Vaccine Research*. 2001.

²⁸ UNAIDS. *Ethical Considerations in HIV Preventive Vaccine Research – UNAIDS Guidance Document*.

²⁹ *Ibid.*

³⁰ *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*

3. PRODUCTION

DEVELOP CANADA'S CAPACITY TO MANUFACTURE VACCINES

25

THE CHALLENGES

Manufacturing vaccines – both for testing and, later, for immunization – is difficult and expensive. Even when a viable vaccine is developed, manufacturing will continue to be an issue.

Manufacturing capacity. There is inadequate production capacity for vaccines in Canada. Once a quality product has been developed, the manufacturer must be able to produce enough vaccine to support clinical trials. Many companies in Canada lack the capacity and resources to manufacture vaccine in sufficient quantities to make it economically attractive.

Quality control and regulatory issues. Early production runs of vaccine may not meet quality standards. This problem occurred with one promising Phase III candidate and delayed approvals and clinical trials by more than a year.³¹ Many are stalled at the process development phase because the world lacks the critical process engineering required to produce vaccines. Local regulatory issues must be in place regarding safety, purity, formulation and adverse effects of any HIV vaccine that reaches the production stage.

Liability. A key challenge is liability protection of vaccine manufacturers. Private companies that have the necessary production capacity may be reluctant to get involved because of liability concerns about adverse reactions to the vaccine. The world has seen effective vaccines withdrawn from the market because of concerns about risk and the growing litigiousness in some developed countries. For example, a pertussis vaccine that could save the lives of hundreds of thousands of children in countries like Bangladesh was withdrawn from the market because one in every 100,000 babies who received it could develop severe bowel obstruction. Although this adverse effect could be prevented or managed with proper hydration, the company was unwilling to accept the risk of being sued. The risk environment in the developed world is affecting the developing world's access to life-saving products. This could be remedied. For example, governments could negotiate to provide public insurance for those injured in vaccines trials in return for pharmaceutical companies making an HIV vaccine available in developing countries at low cost.

³¹ *AIDS Vaccine Advocacy Coalition. How Do You Fight a Disease of Mass Destruction? And other questions on the road to an AIDS vaccine.*

Patents/intellectual property. Many of the elements and processes needed to produce vaccines – such as proteins, basic biotech processes and manufacturing processes – are protected by patents that restrict their use even for research. While patent protection is essential to entice private-sector companies and universities to invest in research, it slows the process of vaccine development and increases its cost. If generic production is permitted once a vaccine is available, there may be less interest from pharmaceutical companies due to low economic incentives. Negotiation of patent rights for generic production should occur when government provides funding to pharmaceutical companies rather than introducing policies after a vaccine is available. Ultimately, the policy systems need to be in place to ensure global access to vaccine products developed in Canada.

Production costs and financial incentives. Because of the risks involved in producing HIV vaccines – including high initial production costs, uncertain markets (i.e., countries that need large quantities of vaccine may not be able to purchase and distribute it) and the pressure to produce a product that will be affordable for developing countries – few private companies will become involved without incentives.

Private-public sector partnerships. Currently, there are no formal private-public sector partnerships for HIV vaccine development. CANVAC had played a role in identifying and setting up partnerships with industry, but further private-public sector partnerships have yet to be formalized.

THE STRATEGY

To enhance Canada's capacity to produce HIV vaccines:

3.1

Create and provide adequate resources to private-public sector partnerships to establish a good-manufacturing-practices HIV vaccine production plant for clinical trial lots and for future vaccine production.

3.2

Explore with Health Canada the feasibility of an expedited regulatory/approval process for HIV vaccines.

3.3

Explore mechanisms that provide compensation for vaccine-related harms that is fair to both HIV vaccines producers and vaccine recipients.

3.4

Explore models to address the intellectual property barriers that slow down HIV vaccines production.

3.5

Develop innovative economic incentives (e.g., a guaranteed market for vaccines, push and pull mechanisms) that will encourage private industry investment.

4. DISTRIBUTION

ENSURE EQUITABLE ACCESS TO HIV VACCINES AT HOME AND ABROAD

THE CHALLENGES

Developing HIV vaccines will not be enough to stop AIDS. The vaccines must be made available, distributed effectively and equitably to, and used by, the people who need them. We must learn from past failures, such as those experienced with antiretrovirals (ARVs) and non-HIV vaccines.

Global access. It usually takes a number of years from the time a vaccine is developed for it to be widely available through immunization programs. In most cases, vaccines are available first and distributed most successfully in countries and regions with the greatest resources, public health infrastructure and political will.

There is a significant gap between our ability to produce effective vaccines and our ability to distribute them and eradicate disease. An example of this failure of political will is measles. It costs only 20 cents U.S. (including the syringe) to immunize a child against measles, yet 800,000 children continue to die each year from measles. Thanks to the recent investment by the Gates Foundation, the measles vaccine is much more widely available, and the number of annual measles-related deaths has dropped by 12.5%.³²

Canada has a responsibility for ensuring that vaccines are available and distributed in other parts of the world. Therefore, one of the challenges may be in balancing domestic and global interests. If supply is an issue, should available supplies be used first in countries with a more widespread epidemic and less access to treatment? Who will make that decision? What role will the communities affected by HIV play in the decision-making process?

Delivery. The speed with which vaccines become available depends on vaccine supply, cost, efficacy and any adverse reactions. There are two reasons that difficult decisions will have to be made about which populations have priority to receive HIV vaccines:

- 1) supply may be inadequate to meet all needs, and
- 2) initial HIV vaccines will be partially efficacious 



PARTIAL EFFICACY

In vaccine research, efficacy refers to the ability of a vaccine to protect vaccinated people against a specific infection or disease, at the optimal dosage and schedule in a given population. A vaccine may be tested for efficacy in Phase III trials if Phase I and Phase II trials show it to be safe and promising. Partial efficacy means that a vaccine does not confer immunity on all participants who receive the vaccine. Technically, all vaccines are partially efficacious because none can 100% fully guarantee that a person will not become infected if he or she is exposed to the infectious agent.

³² www.gatesfoundation.org

In deciding who and how many people should receive a vaccine, public health authorities take into account the risk of exposure to the infectious disease, the risk of adverse reactions and the efficacy of the vaccine. For example, should all gay men in Canada be offered vaccination? All people who inject drugs? All Aboriginal people? What criteria will help target immunization programs?

Uptake. Even in countries where vaccines for diseases such as influenza, measles and tetanus are widely available through voluntary programs, a significant proportion of people who could benefit have not been immunized.

In Canada, the ability to deliver HIV vaccines effectively will depend on the capacity to reach marginalized populations, protect their human rights, build their trust in the health system and encourage their willingness to use the vaccine. Are there particular strategies that should be used to reach people who inject drugs and encourage vaccine uptake? People who are homeless? Youth? Innovative work is already being done in Montréal and Vancouver to distribute and promote the use of other adult vaccines (e.g., hepatitis A and B) to marginalized people at high risk, and this expertise should be used to help develop effective distribution strategies for HIV vaccines. Canada's National Immunization Strategy may also provide useful information to guide distribution and uptake. There are lessons to be learned from obstacles to vaccine compliance in the general population with respect to common childhood vaccines.

Encouraging the appropriate uptake and use of HIV vaccines will create complex policy and education issues for all jurisdictions. With HIV, vaccine uptake may be affected by the fact that some vaccines may target certain strains of HIV and only be appropriate for some people. Helping people understand the difference between preventive and therapeutic vaccines will also present a challenge. Therapeutic vaccines will not confer the protection of a preventive vaccine, so prevention/harm reduction education must be a vital component of any vaccination program. On the other hand, therapeutic vaccines may play a preventive role by helping to reduce viral load and make transmission less likely.

THE STRATEGY

To ensure timely and appropriate delivery and distribution of vaccines in Canada and globally:

4.1

Define and create an active role for Canada in ensuring that developing countries have equitable and timely access to vaccines. Learning from failures to deliver ARVs in the developing world until long after developed countries had access to them, capacity for vaccine distribution must be assured in advance of an HIV vaccine becoming available.

4.2

Work with international partners and other countries to develop a strategy for subsidizing and supporting vaccine distribution in the developing world, including addressing the delay in approving new health products.

4.3

Bring together HIV-affected communities, public health, health care providers, vaccine manufacturers and governments to urge the National Advisory Committee on Immunization to develop recommendations to public health authorities on how to administer HIV vaccines in Canada. The recommendations will be built on evidence-based criteria for determining who will receive vaccines; on how vaccines will be distributed and promoted, based on different scenarios (e.g., vaccine supply, vaccine efficacy); on the settings in which vaccines will be delivered; on how adverse events (e.g., reactions, side effects) will be monitored; on how liability will be managed; and on how the immunization program will be evaluated.

4.4

Link with the Canadian HIV Strain and Drug Resistance Program, a systematic surveillance of HIV genetic variability in Canada that can inform vaccine research and development. The surveillance system would collect data on the prevalence and incidence of HIV subtypes and other determinants of subtype diversity in Canada to inform vaccine strategies, since the efficacy and effectiveness of vaccines will likely be subtype-specific.

4.5

Ensure that all health jurisdictions (federal, provincial/territorial) provide for coverage of HIV vaccines in their formularies.

4.6

Identify barriers that may prevent uptake of HIV vaccines in different populations (e.g., lack of information about vaccines, stigma and discrimination associated with taking the vaccine, overestimating the risk of vaccination, underestimating the risk of HIV infection), and develop strategies to overcome them.

4.7

Conduct a comprehensive review of best practices in access to and delivery of existing vaccines, focussing particularly on hard-to-reach populations.

4.8

Develop and assess innovative approaches to delivering HIV vaccines to hard-to-reach populations, including involving and preparing people living with HIV/AIDS and people at risk.

4.9

Develop policies and strategies to overcome any potential regulatory or financial barriers to delivering vaccines.

4.10

Engage community-based organizations in preparing communities for HIV vaccines. For example, education must be provided to community members in order to create a culture that is welcoming to vaccination in the population at large, in health care workers and in risk populations.

4.11

Reinforce existing prevention strategies for both HIV-negative and HIV-positive individuals to accompany vaccine distribution, placing vaccines within a continuum of prevention, diagnosis, care, treatment and support. Community-based organizations already serving vulnerable populations and people living with HIV should take a lead in developing and implementing the prevention strategy.

5.

COMMUNITY ENGAGEMENT

ENGAGE CANADIANS IN VACCINES RESEARCH, PRODUCTION AND DISTRIBUTION

33

THE CHALLENGES

Developing HIV vaccines will be difficult, costly and time-consuming. Carving out a role for Canada in vaccines research, production and distribution will require sustained community support, both from the general public and from the communities most affected by HIV. Communities must be engaged through all phases of vaccine research, from discovery to trials and through to production and distribution. Communities (both in terms of the general public and vulnerable groups) must be aware of the possible impact and benefits of vaccines.

There are three important aspects of community engagement: 1) the general public supporting expenditure of resources; 2) vulnerable populations that would most likely be targets for testing and receiving the vaccines; and 3) organizations working with those populations.

The public. The public must be engaged to raise their awareness of the need for HIV vaccines and the necessary efforts to develop them and maintain support for vaccine research efforts. People need to believe that HIV vaccines are important and the investment in them worthwhile. Canadians must understand the need for well-funded, long-term Canadian HIV vaccine initiatives that are linked to global vaccine efforts and see that this kind of sustained investment will save lives, provide a more cost-effective response to HIV, help create a world without AIDS, build research capacity within Canada, contribute to global health and put us in a stronger position to fight other illnesses. The public should be educated to see HIV vaccines as part of Canada's ongoing commitment to health and human rights.

Those involved in HIV vaccine initiatives must be able to communicate to the public a strong rationale for making HIV a priority. HIV vaccine activists and researchers need to maintain public interest in preventive vaccine research as ARVs improve and as first generations of therapeutic vaccines come out. The general public needs to have accurate and realistic messages about the challenges of developing an HIV vaccine and the importance of adequate resources to support the efforts to develop a vaccine. 

People living with or at risk of HIV. People living with or at risk of HIV in Canada are key to the success of this plan. They are the people who will participate in clinical trials, help direct the trials and eventually be the first recipients of vaccines. They are also the people who will help design trials, advocate for political commitment and funding for

"In today's global economy, a disease that has killed more than 30 million people is everyone's problem, and every company's responsibility."

Richard Holbrooke, President of the Global Business Coalition on HIV/AIDS (Agence France-Presse, October 9, 2005)

vaccines, and influence whether vaccines will be accepted and used. Their knowledge and experience can help researchers learn from the lives of people living with HIV or at risk and use that information to develop better study protocols and improve practical, logistical aspects of vaccine trials.

To fulfil that role, they will need access to information in an understandable form, and they will need to develop the capacity to influence decision makers, shape public policy, and lobby governments, the research community and the public.

Through the community advisory boards (CABs) established to guide the first vaccine trials in Canada, people living with or at risk of HIV have already been engaged, but more must be done. Although the CABs were effective, they had limited capacity to disseminate information. CABs are one model that has been used to represent the interests of the communities, to help recruit and retain trial volunteers, and to liaise between community members and researchers. CAB members should be nominated to represent trial volunteers and protect their rights. While CABs, with some adjustments, may be an effective way to engage people living with HIV/AIDS and people at risk, there may also be other models – ones that can forge strong links between the research and community efforts to advocate for effective prevention and treatment – that should be explored. In general, the role of “interpreting” science for people who will participate in or benefit from vaccine trials will likely fall to community advocates, such as community-based researchers, who understand both the research world and the culture and information needs of people living with or at risk of HIV. While partnership between study participants and researchers is the goal, some vulnerable populations may be unwilling to be involved with a community board. This should not preclude them from participating in trials.

Because the first HIV vaccines may be only partly effective and are not expected to confer full immunity (i.e., they may be effective only against certain strains of the virus), people living with or at risk of HIV must be educated about what a particular vaccine can or cannot do and understand its limitations. It is vital that people with HIV and populations at risk understand that HIV vaccines are only one part of a comprehensive prevention and treatment strategy. Every effort must be made to ensure that people understand the limitations of a partially efficacious (or low-efficacy) vaccine and ensure that they maintain their treatments and other preventive measures, such as safer sex and safer drug use. To encourage long-term, effective, appropriate use of vaccines, Canada must know more about the attitudes and practices of people living with HIV/AIDS and populations at risk. Canada must take into account the impact of both vaccines and people's expectations (i.e., vaccine optimism) on other prevention/education efforts.

Community-based organizations. Community-based AIDS service organizations face multiple challenges with respect to understanding and engaging in HIV vaccine work. The challenges include being chronically under-resourced and viewing vaccine research and development as remote and advocacy unattainable in comparison to more immediate service provision demands.³³ National NGOs need to take a lead and help build the capacity of local community-based AIDS service organizations to engage in HIV vaccines education, advocacy, trials, etc. These organizations feel that leadership on vaccines advocacy has to come from national constituency-based organizations and committed grass-roots advocates because most local groups do not currently have that capacity.³⁴ X

The Canadian HIV Vaccines Plan should be used by all stakeholders, including community-based organizations, as a national monitoring tool to measure progress and to assign responsibility for key projects. Researchers should disseminate their basic and clinical science results in large community fora, and in ways that community members are able to understand, in order to build literacy on vaccine research and stimulate dialogue on access to vaccines while advocating for increased investments in vaccine research.

During the discovery phase, community-based organizations should be starting to sell the idea of building understanding and political commitment. The organizations should be included in partnership agreements along with researchers, industry and government, specifying how communities will contribute to providing support for discovery efforts, raising the profile of vaccine research, including vaccine research in provincial health strategies, and sharing information with community members about the benefits and risks of a vaccine.



"We need to find a way to reach out to a broader community and find people who love to talk about basic science and then bring them into the HIV movement so that we get to the point where the conversation about HIV vaccines, microbicides, and new medicines is an informed scientific conversation. There has to be a certain level of scientific literacy within communities because otherwise they can be exploited by quacks or people who wish to misuse science for commercial or political ends."

Zachie Achmat
Interview with Kristen Jill Kresge
VAX 3(12), December 2005

³³ Canadian AIDS Society (2005). *HIV vaccine preparedness: Capacity-building needs of community-based AIDS organizations*.

³⁴ *Ibid.*

THE STRATEGY

To engage the public, people living with or at risk of HIV, and community-based organizations at all levels in efforts to develop, test and deliver HIV vaccines, a Canadian HIV vaccines plan would:

5.1

Assess current public attitudes towards HIV vaccines and develop an education program that would raise awareness of the importance and benefits of investing in vaccine research.

5.2

Promote vaccines as one part of a comprehensive approach to HIV prevention and treatment and reinforce the need for other prevention/education initiatives and the importance of reducing risk behaviours.

5.3

Encourage ongoing dialogue among researchers and community advocates to enhance both researchers' understanding of community issues/needs and community support for vaccine development.

5.4

Continue to develop effective mechanisms to support community involvement in vaccine research, such as CABs and human rights education. Building on lessons learned from CABs, explore new models for engaging communities in vaccine trials.

5.5

Build the capacity of people vulnerable to HIV to lobby for funding and policies to support a vaccine program in Canada, participate in community advisory boards and other mechanisms, influence research priorities, assist in ethical recruitment, provide education within their communities, and participate in efforts to ensure access to vaccines for those communities that need them most, and support them in these activities.

5.6

Develop specific, targeted education, information and support programs to protect the human rights of trial participants.

5.7

Develop specific education programs to promote appropriate use of vaccines and counter unwarranted vaccine optimism.

5.8

Build community-based research capacity in the area of HIV vaccines to increase community-based understanding of barriers, challenges and ethical issues in testing and distributing vaccines; development of community-based strategies to maintain behavioural prevention; and development of public education strategies.

5.9

Ensure that communities understand the complexity and the nature of the long-term, incremental progress of the HIV vaccine research process. The message must be given that even if a candidate vaccine proves non-efficacious, their participation in the trial was valuable. The message must be that "trials never fail"; some information is always produced about the immune system that is scientifically useful for future development of vaccines. Trial participants should be informed of the benefits of their contribution from a science perspective as well as a community-level learning perspective.

5.10

Ensure that populations that could benefit from a vaccine have clear information about both its benefits and its limitations in a form and language that is easily understood.

5.11

Use the experience of existing vaccine programs for people living with or at risk of HIV to help identify effective communication and uptake strategies.

5.12

Build on Canada's strength in social research by funding research that supports effective vaccine development and use (e.g., assessing the acceptability of vaccines, identifying any misperceptions that people living with or at risk of HIV may have, helping identify sub-groups of people at high risk of HIV who should be actively recruited to participate in trials, developing effective recruitment and retention strategies, monitoring the attitudes and behaviour of trial participants, assessing the impact of trials on risk behaviour in the communities affected by HIV, and identifying social factors that affect the introduction and distribution of vaccines.³⁵)

³⁵ Rosengarten M, Murphy D. *Making Connections. HIV Vaccines and Microbicides: A Social Research Agenda*. National AIDS Trust.

6. POLITICAL LEADERSHIP AND FINANCIAL COMMITMENT

PROVIDE LONG-TERM, DEDICATED LEADERSHIP AND FUNDING

39

THE CHALLENGES

All the steps involved in developing HIV vaccines – discovery, trials and testing, production, distribution, community engagement – will require leadership and financial commitment. The vision of all leaders must be to develop and deliver safe, efficacious vaccines that are globally accessible.

Leadership. Developing HIV vaccines will take time. (Vaccine development usually takes an average of 14 to 19 years, not including time for production and distribution.³⁶) During the discovery and testing process, there will be setbacks that may cause people to question the investment in HIV vaccines. There will be pressure for funds to be used for other, more immediate health needs. There will be competing demands for the attention of policy makers, funders, researchers and communities. There may also be changes in government and policy that could affect Canada's ability to stay the course. It is vital for the public, people living with or at risk of HIV, policy makers and funders to understand that even when trials are not able to demonstrate vaccine efficacy, they still help develop useful knowledge (e.g., that a certain category of vaccine candidates does not work, therefore research should focus in other areas) that will eventually lead to HIV vaccines or to other discoveries. 

Long-term research programs require long-term commitment and political leadership. Everyone with a stake in HIV vaccines – policy makers, community, people living with HIV and those at risk, public health, health care professionals, NGOs, private sector, researchers and clinicians – should be actively engaged in explaining the potential for HIV vaccines, the need for an ethical approach to vaccine development and the strengths that Canada can bring to the global effort. Stakeholders should work together to keep at the forefront of Canada's HIV efforts, giving voice to the need and advocating for sustained support and funding. They should be engaged in lobbying for coherent, supportive public policy. Clinicians, researchers and the private sector must be prepared to devote time and expertise to vaccine development.

Financial Commitment. Developing HIV vaccines will also require money. A coordinating structure is needed to create a multisectoral approach to vaccine planning, one that will allow us to provide dedicated, long-term funding for research at home and abroad and to develop policies that support an effective HIV vaccine program. At the current time,



"The world needs an AIDS vaccine more urgently than it needs any single medical discovery, and Africa needs it more than any other part of the world. But for some inexplicable reason, the consuming enthusiasm, the obsessive drive, the sheer, unrelenting passion for a vaccine is simply not riveting the world at large as should be and must be the case. I would argue that the same kind of extraordinary commitment, in country after country, to achieve '3 by 5', and then to progress to universal treatment, is exactly what has to happen in the pursuit of a vaccine."

*Remarks by Stephen Lewis, UN Special Envoy for HIV/AIDS in Africa
AIDS Vaccine 2005 International Conference
Delivered at the opening ceremony,
Montreal, Canada, September 6, 2005*



THE MINISTERIAL COUNCIL ON HIV/AIDS
RECOMMENDS THAT:

"...Canada, in addition to strengthening support for Canadian HIV-related research, including through developing a national HIV vaccine plan and strengthening research into microbicides, increase its contribution to international HIV vaccine and microbicide research efforts.

"... DFAIT, through its bilateral and multilateral relations, promote international HIV vaccine and microbicide research efforts."

*Meeting the Challenge: Canada's Foreign Policy on HIV/AIDS - With a Particular Focus on Africa
prepared by John Foster and David Garmaise for the
Ministerial Council on HIV/AIDS, September 2003*

³⁶ IAVI. *The state of global research.*
<http://www.iavi.org>, December 2004.

global spending on HIV vaccines is less than 1% of global spending on all health product research and development.³⁷ In 2000, IAVI called for a threefold increase in global spending, from \$350 million to \$1.1 billion annually. In 2004, IAVI estimated that about \$650 million a year is spent on vaccine research and that private-sector spending is just \$100 million each year, mainly because of a lack of incentives to invest in HIV vaccines, the scientific challenges of HIV vaccine research, and the fact that the countries that need the vaccines most are least able to pay.³⁸ Intellectual property issues must be proactively addressed by the various government departments involved (Public Health Agency of Canada, Department of Foreign Affairs and International Trade, Industry Canada, etc.) well in advance of a vaccine candidate being ready for production.

Canada should have both a strong domestic and a global vaccine research program because they offer distinct and complementary contributions to vaccine development efforts. On the international front, since 2001 Canada has contributed a total of \$62 million to IAVI and \$5 million to the African AIDS Vaccine Plan. However, on the domestic front, there is currently no targeted funding for an HIV vaccines research program. At this point, CIHR supports and encourages individual HIV vaccines research projects through priority announcements for the open CIHR competitions. Priority announcements support proposals in priority research areas that are highly rated but not funded through the open competitions. Through open competitions and priority announcements, CIHR supports HIV vaccine research through general research grants, funding for clinical trials, personnel awards and Canada Research Chairs. The chart below summarizes vaccines research funding between 2001-02 and 2006-07. CANVAC, the only coordinated effort in HIV vaccines in Canada, ended in March 2006. In the past, CANVAC has devoted some of the funding it receives from CIHR to HIV vaccines research and development. In 2005, CANVAC devoted just over \$800,000 of its funding to therapeutic and preventive HIV vaccines research.

A shortcoming in the past has been limited (and not readily accessible) funding for researchers in Canada to collaborate with international research partners. A positive development was the November 2005 announcement of \$3 million to support international partnerships between domestic and African researchers, to be administered through the Global Health Research Initiative, a collaboration among CIDA, the IDRC, CIHR and Health Canada.

CIHR INVESTMENT SUMMARY
VACCINE RESEARCH

FISCAL YEAR	01-02	02-03	03-04	04-05	05-06	06-07
RESEARCH GRANTS	1,336,977	1,371,203	1,664,759	1,552,800	2,027,676	1,727,360
TRAINING AND SALARY AWARDS	390,140	460,388	483,114	521,375	544,000	495,916
INFRASTRUCTURE SUPPORT*	3,525,000	3,525,000	7,725,000	7,809,000	7,895,000	4,457,000
TOTAL INVESTMENT	5,252,117	5,356,591	9,872,873	9,883,175	10,466,676	6,680,276

* Only a portion of the infrastructure funding for CTN and CANVAC directly supports HIV vaccine research

It is vital that Canada continue to contribute to global vaccine efforts, but it is equally vital that Canadian governments, research funding bodies and the private sector provide dedicated, sustained, long-term support for vaccine programs in Canada. We must do both if we are to fulfil our obligations.

³⁷ *Ibid.*

³⁸ *Ibid.*

Governments and other funding organizations must be willing to devote resources to vaccine development at home and abroad and to protect those resources over time. There is currently no targeted HIV vaccine research funding, other than indirect research funding for Canada Research Chairs under CANVAC, which supports their overall research programs, not only HIV/AIDS. In addition, this funding comes from CIHR core funding rather than the Federal Initiative to Address HIV/AIDS in Canada. Likewise, the CTN receives CIHR infrastructure support for setting up HIV/AIDS trial clinics but not for vaccine discovery research.

Canada needs to build a larger body of vaccine researchers and develop dedicated funding for vaccine research, both in terms of personnel training and research grants. While some researchers receive grant funding based on scientific merit out of general funds, dedicated HIV vaccine research funding would allow more targeted research initiatives to strategically focus on Canada's key contributions in HIV vaccine discovery and testing.

THE STRATEGY

To ensure leadership and financial commitment for HIV vaccine development in Canada and globally, a Canadian HIV vaccines plan would:

6.1

Bring together representatives of government, community, people living with HIV/AIDS and those at risk, industry and research to form a multisectoral coordinating body responsible for providing leadership, implementing and monitoring Canadian HIV vaccines efforts and developing links with global vaccine efforts.

6.2

Develop a federal government business plan to ensure a long-term, dedicated funding program for HIV vaccines research domestically and internationally. Explore leveraging opportunities with provincial and other health research funding partners (e.g., Ontario HIV Treatment Network, Alberta Heritage Foundation for Medical Research, Fonds de la recherche en santé du Québec, National Alliance of Provincial Health Research Organizations).

6.3

Bring together different government departments, such as the Public Health Agency of Canada, Health Canada, Canada Revenue Agency, International Trade Canada, Industry Canada and others to develop strategies and incentives to actively engage the private sector in participating in Canadian HIV vaccines efforts.

6.4

Ensure Canadian HIV vaccines efforts are strategically aligned with other HIV/AIDS strategies, including Canada's International Policy Statement, *Leading Together: Canada Takes Action on HIV/AIDS (2005-2010)* – the pan-Canadian HIV action plan, the Federal Initiative to Address HIV/AIDS in Canada and the strategies currently being developed by CIDA and Foreign Affairs Canada.

6.5

Work with global vaccine research initiatives (such as the Global HIV Vaccines Enterprise) to ensure that Canada's contributions complement and fill gaps in global knowledge development and policy making.

APPENDIX A

TIMELINE PATH OF ACTIVITIES FOR A CANDIDATE VACCINE

42

TIME			
DISCOVERY	TRIALS AND TESTING	PRODUCTION	DISTRIBUTION
Assign clinical trial sites			
Develop a community ethics plan			
Negotiation of patents and regulatory frameworks			
Capacity building in developing countries for production and distribution infrastructure			
Community engagement			
Political leadership and financial commitment			

Many elements of vaccine work must happen concurrently. For example, community engagement and financial commitment need to happen all along the continuum of vaccine research, testing, production and distribution. From the perspective of discovery, finding a candidate vaccine takes priority. At the same time, Canada should establish a nationally based vaccine preparedness cohort, with funding available for Phase I and II clinical trials of a putative national candidate vaccine within the next few years. Community-level education to promote participation in clinical trials needs to take place alongside efforts to discover a vaccine. Agreement regarding manufacturing, distribution and intellectual property issues must be reached in advance of a vaccine being discovered. Finally, we cannot wait until a vaccine is available to build the infrastructure for production and distribution of a new vaccine. Capacity building for vaccine distribution must be undertaken in developing countries before a vaccine becomes available.