Canadian and Global HIV Vaccines Priorities

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Presentation Outline

- Context
- Global HIV Vaccines Priorities
- Canadian HIV Vaccines Priorities
- Regulatory Affairs activities

Section I: Context

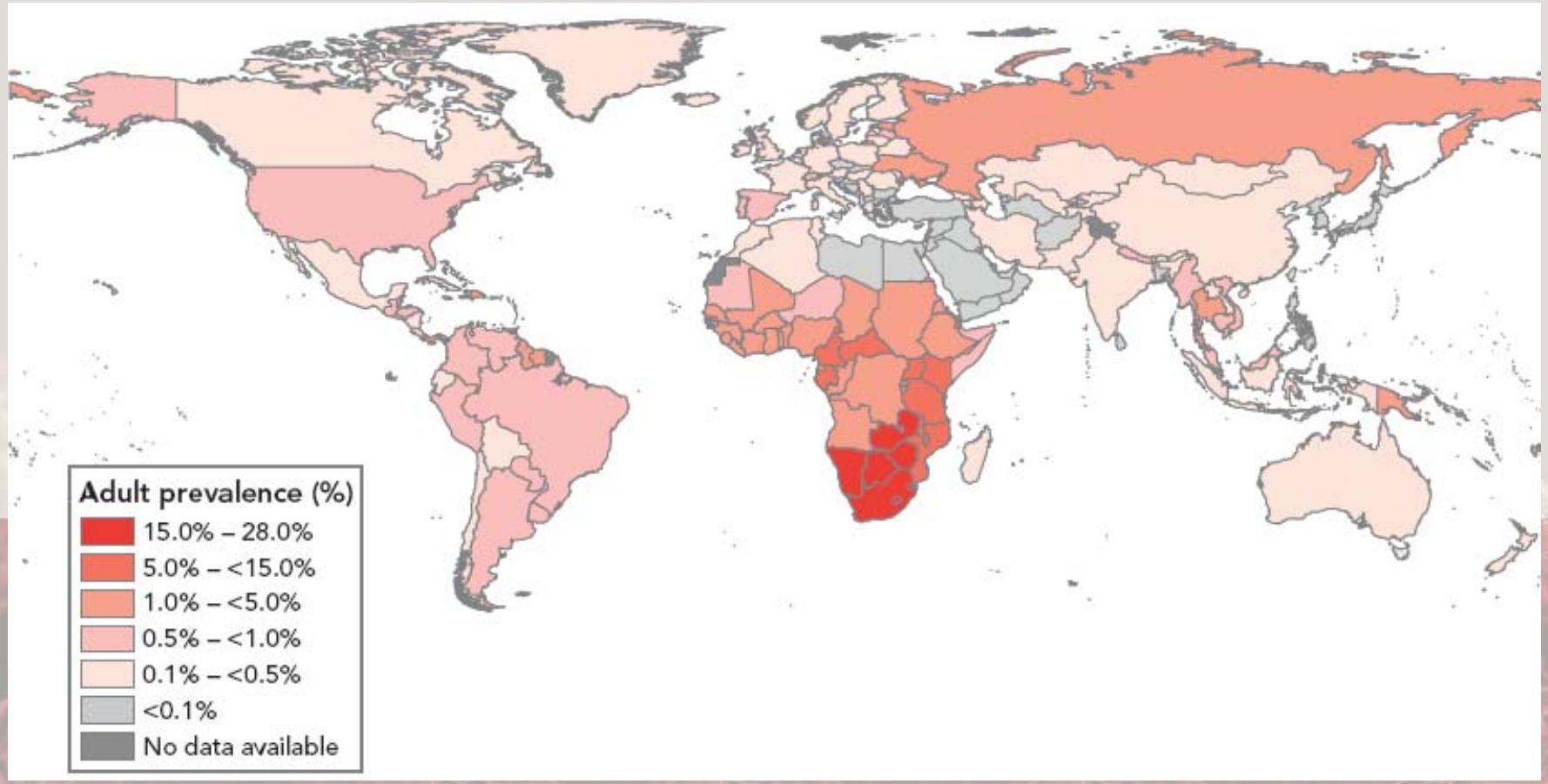
Context -- State of the Epidemic (2007)

- 33.2 million people living with HIV
- 2.5 million new HIV infections
  - More than 7400 new infections every day
- 2 million deaths due to complications from AIDS
  - More than 5700 deaths every day
- Complications from AIDS remains the leading cause of death in adults in Sub-Saharan Africa
- Almost 61% of adults infected with HIV in Sub-Saharan Africa are women

Source: **UNAIDS**, 2007/2008

The Global HIV Epidemic

Adult HIV Prevalence, 2007



Source: **UNAIDS**, 2008

Comprehensive Response to HIV/AIDS

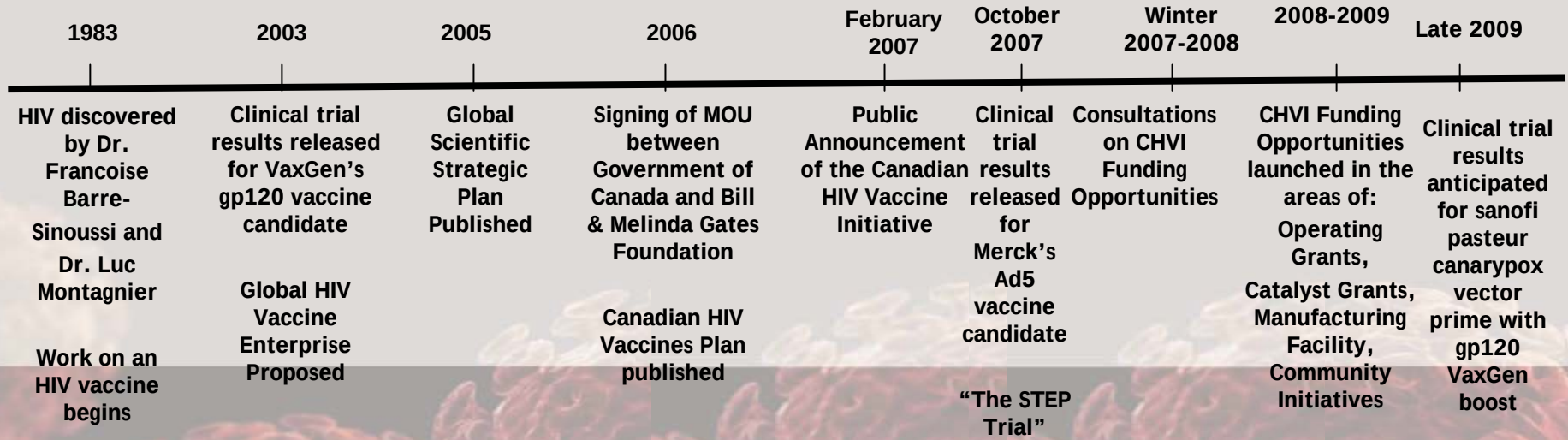
- The world needs an integrated and comprehensive plan that includes short, medium, and long term solutions

- Short-Term:
  - Expand currently accepted treatment modalities
  - Prevent sexual transmission (e.g. behavioral, condom usage, male circumcision)
  - Prevent blood-borne transmission (e.g. needle/syringe exchange, treatment, PrEP)
  - Prevent mother-to-child transmission (e.g. ARVs)

- Medium-Term:
  - Development of microbicides, PrEP

- Long-Term:
  - A safe and effective preventative vaccine

Timeline of Historical Global/Canadian HIV Vaccines-Related Events



Historical Events (Cont'd)

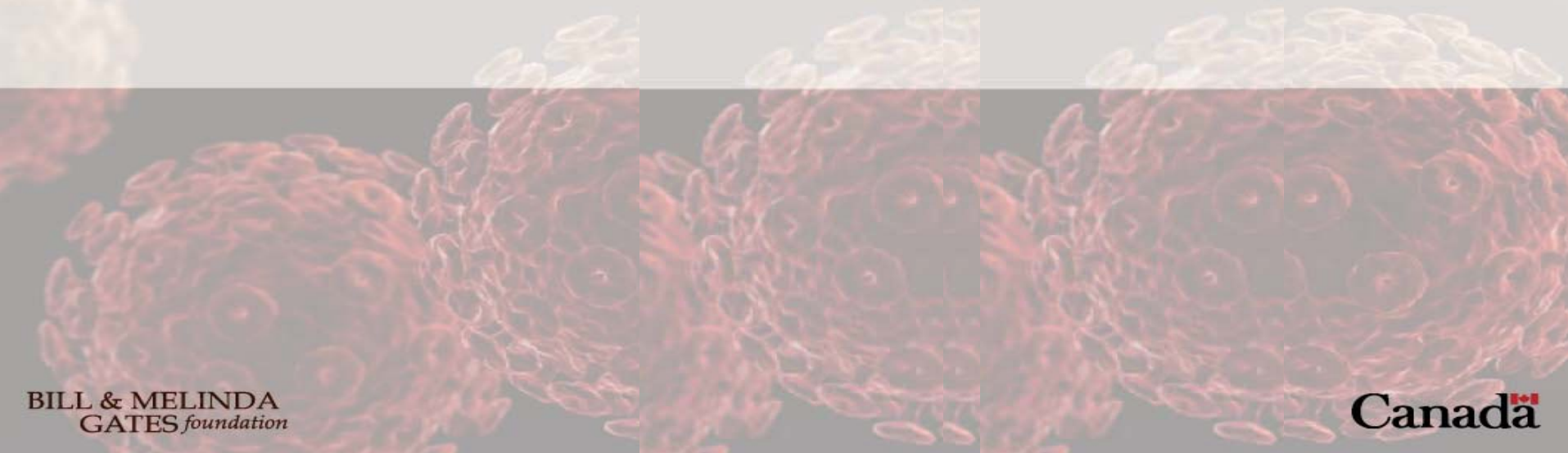
- HIV discovered by Dr. Francoise Barre- Sinoussi and Dr. Luc Montagnier in 1983 (awarded Nobel Prize in 2009)

- Different types of vaccines have been developed and tested over the past two decades – For example:
  - VaxGenEnv gp120 protein – humoral immunity (2003) -- Phase 3 study elicited type-specific, but not broadly reactive, antibodies; No efficacy
  - Merck Ad5-Gag/Pol/Nef vectors – cellular immunity (2007) -- Phase 2b study elicited cellular immunity as measured by IFN-g ELISPOT assays; No efficacy, possible enhanced acquisition in uncircumcised men with pre-existing anti-Ad5 immunity
  - Thai canary pox prime, VaxGen boost – humoral and cellular immunity (2004-) -- Phase 3 study, 16,000 participants enrolled, trial ends July 2009; Results in September/October 2009

Current Challenges

- Scientific: Extensive sequence diversity; no method exists to elicit broadly reactive Nabs; immune correlates of protection unclear; lack of robust endpoints for vaccine trials; viral evasion of humoral and cellular immune responses; lack of a robust animal model
- Limited industry engagement
- Political, ethical, regulatory challenges

Section II:
Global HIV Vaccines Priorities



Global Priorities

- Scientific: increasing understanding of human immune response to HIV and candidate vaccines; designing immunogens capable of eliciting broadly reactive long-lived immune response; Incorporating systems biology / high throughput technologies /computational biology; developing mechanism-based endpoints for clinical investigation.
- Human resources: attracting and retaining the brightest young researchers.
- Collaboration and partnership: increasing international collaboration between scientists, governments, and funders; increasing dialogue between clinical and preclinical researchers; and seeking active partnerships between academia and industry.
- Regulatory: increasing capacity in developing countries.
- Communications: public awareness and support.
- Funding.

New Minds, New Ideas: Engines of Discovery

- Young researchers bring energy, creativity, and new approaches
- Investigators from countries most affected by HIV offer new insights and perspectives
- Researchers from other fields bring new technologies

Global HIV Vaccine Enterprise

Created by the world's leading funders of HIV/AIDS research to articulate the fastest way forward to a safe and effective preventive HIV vaccine

BILL & MELINDA GATES *foundation*

Canada

How Does The Enterprise Achieve Its Mission?

- **Develop and maintain the Global Strategic Plan**
  - Catalyze efforts; identify opportunities; address obstacles; monitor progress
- **Serve as a neutral convener, catalyst, and honest broker**
- **Mobilize support for increased resources**
  - Target significant new resources to priority areas in strategic plan
- **Promote greater collaboration and coordination**
  - Encourage faster, more efficient ways for researchers and funders to share information

Scientific Strategic Plan

PLoS Medicine, **February 2005**

- Developed by 140 scientists from 15 countries

Open access, freely available online

Policy Forum

The Global HIV/AIDS Vaccine Enterprise: Scientific Strategic Plan

Coordinating Committee of the Global HIV/AIDS Vaccine Enterprise

Introduction

In June 2005, an international group of scientists proposed the creation of a Global HIV Vaccine Enterprise [1]. The authors invited discussion of this proposal, and challenged scientists to identify new strategies and mechanisms to accelerate the global effort to develop a safe and effective HIV vaccine. This paper describes the processes that led to agreement on the major roadblocks in HIV vaccine development, summarizes current scientific priorities, and describes an initial strategic approach to address those priorities. Specific research is not prescribed. Rather, the intent is to stimulate both researchers and funders to explore new, more

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

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

The motivation behind the proposal for a Global HIV/AIDS Vaccine Enterprise was the recognition that development of an HIV vaccine remains one of the most difficult challenges confronting biomedical research today [2,3]. Fortunately, scientific progress has created new opportunities that could be harnessed more effectively through global coordination and collaboration. These new opportunities include an expanded HIV vaccine candidate pipeline, improvements in animal models, a growing database from clinical trials, and the availability of new quantitative laboratory tools that make comparisons among vaccine studies feasible. Confronting roadblocks and harnessing the opportunities requires an effo magnitude, intensity, and desi out precedent in biomedical with the Human Genome Pro potentially useful model [4]. specifically, the critical scienti sights generated by the creati individual investigators, as wel groups and individual networ be significantly augmented by erly organized, managed, and atized international effort tar the design and clinical evalua novel HIV immunogens. An i tional collaborative effort tha dresses a shared scientific pla provides information exchang groups, links clinical trials wit ardized laboratory assays and tion in animal models, applies knowledge to improvements i design in an iterative manner supports a transparent proces decision making in all aspects vaccine discovery, design, deve and clinical testing will prove success.

The Global HIV/AIDS Vacc terprise represents a novel pa seek and identify internationa ment on the critical roadbloc developing an HIV vaccine an creating a shared scientific pl addresses those roadblocks (se The Enterprise proposes to co efforts at a global level, facilit common tools and technologi help ensure access to optimiz sources. Furthermore, the Ent approach is a way of behaving global community of problem more openly sharing informat suring that the shared scientif

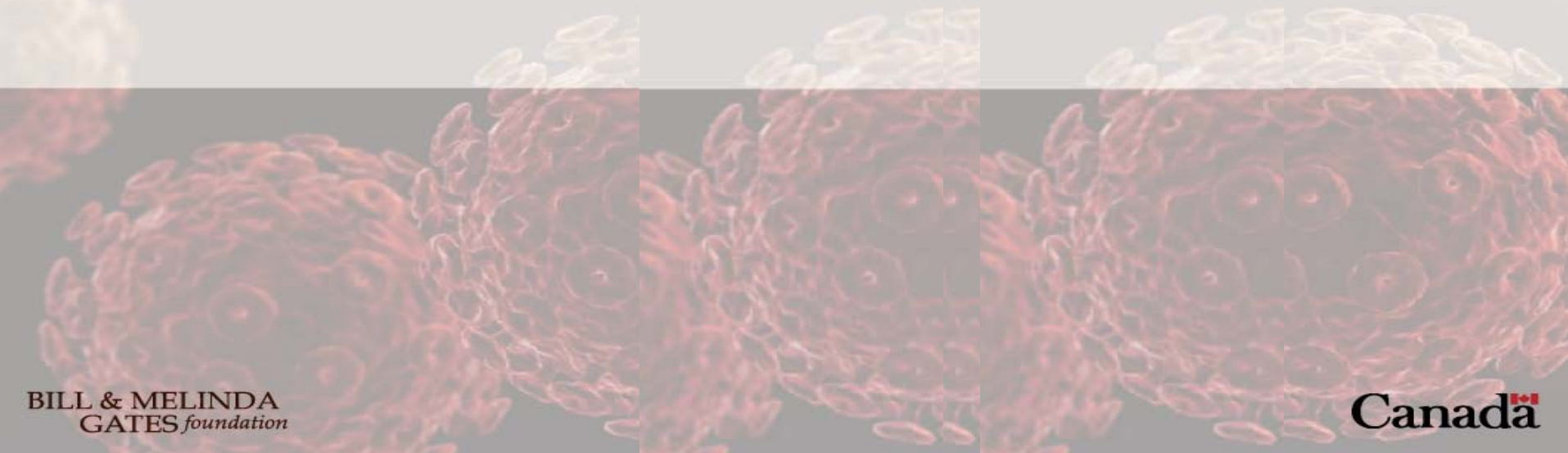
The Policy Forum allows health policy makers around the world to discuss challenges and opportunities for improving health care in their societies.

PLoS Medicine | http://www.plosmedicine.org 0111

Six Priority Areas:

1. Vaccine discovery
2. Laboratory standardization
3. Clinical trials capacity
4. **Regulatory capacity**
5. Intellectual property
6. Product development and manufacturing

Section III:
Canadian HIV Vaccines Priorities



Canada's Involvement in Global HIV Vaccines Efforts

- 2000 to 2006 – Government of Canada invested over $93 million to support Canadian and international HIV vaccine research.

- Spring 2006 – Multi-stakeholder "Canadian HIV Vaccine Plan: Towards a World Without AIDS" was released.

- August 2006 - Memorandum of Understanding (MOU) signed between the Government of Canada and the Bill & Melinda Gates Foundation to formalize a collaboration to strengthen global efforts to accelerate the development of HIV vaccines.

- February 2007 - Canadian HIV Vaccine Initiative was announced by the Prime Minister and Bill Gates.

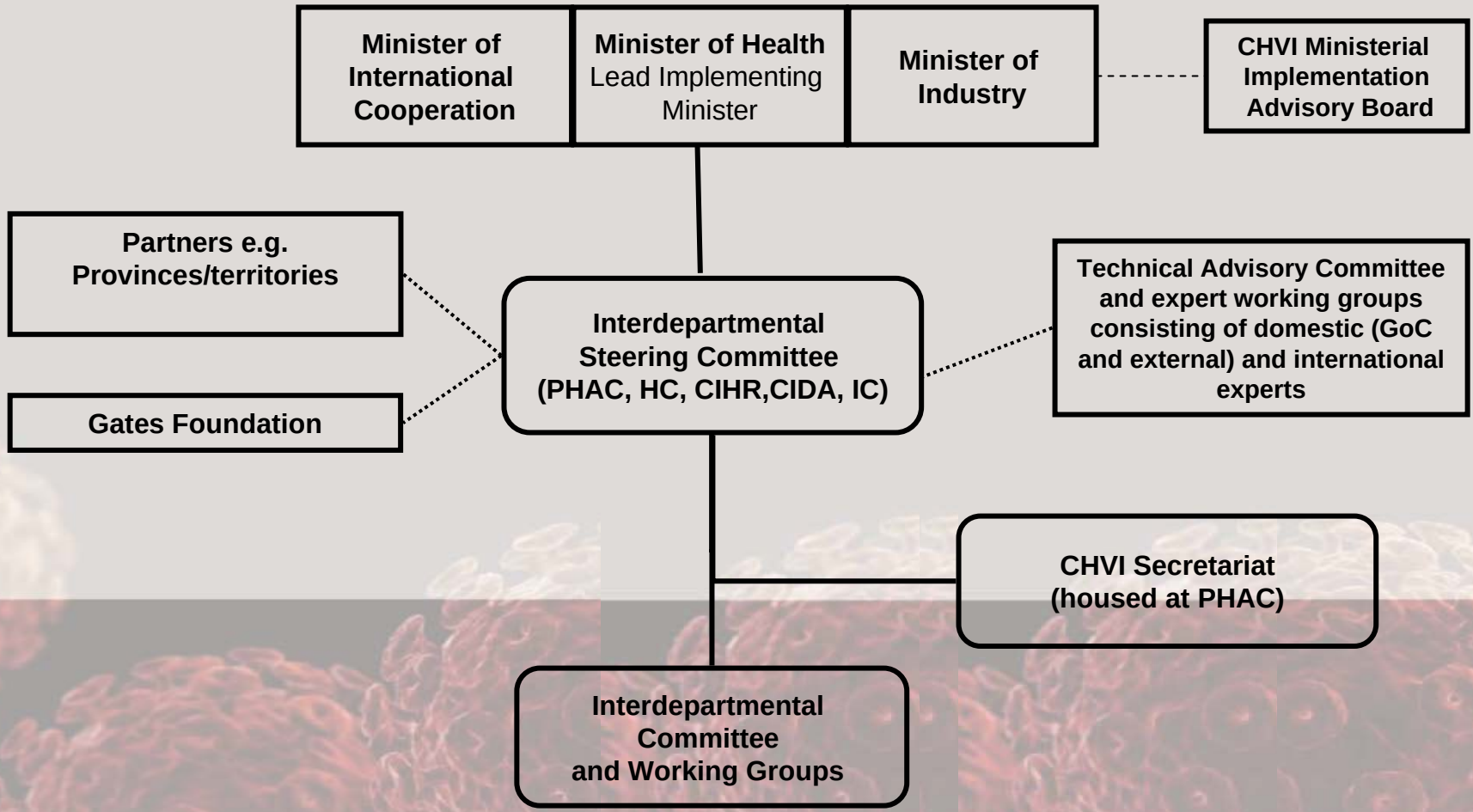
Canadian HIV Vaccine Initiative (CHVI)

- Goals:
  - Coordinate Canadian domestic and international contribution to Global HIV Vaccine Enterprise
  - Accelerate development of a preventive HIV vaccine
  - Collaborate with key global and domestic partners

- Horizontal Initiative involving the Canadian International Development Agency, the Public Health Agency of Canada, Industry Canada, the Canadian Institutes of Health Research and Health Canada

- CHVI is supported through a Government of Canada five-year investment of $111 million Cdn. and funding from the Bill & Melinda Gates Foundation amounting to $28 million Cdn. for a total of $139 million Cdn.

CHVI Governance Structure



Guiding Principles

- **Strategic coordination and integration** – alignment with the Global HIV Vaccine Enterprise Scientific Strategic Plan.
- **Collaboration and engagement** – active involvement and partnerships among governments, private sector, academic researchers, NGOs, civil society and people living with HIV/AIDS.
- **Global Accessibility** - ensure access to future vaccines to people most in need (low- and middle-income countries)
- **Accountability and transparency** - multi-sectoral initiative implemented through open, transparent processes

CHVI Priorities

Global Priorities

Vaccine Discovery

Laboratory Standardization

Product Development and Manufacturing

Clinical Trial Capacity

Regulatory Capacity

Intellectual Property Issues

CHVI Discovery and Social Research

CHVI Priorities

CHVI Pilot Scale Manufacturing Capacity for Clinical Trial Lots

CHVI Clinical Trials Capacity Building and Networks

CHVI Policy and Regulatory Issues, Community and Social Dimensions

Basic research

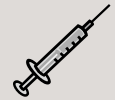
Applied research

Preclinical development

Process engineering

Small scale human clinical trials

Large scale clinical trials



Licensure & delivery

Post-market surveillance

Scientists study the basics of HIV/AIDS and the immune system

Basic research is translated into the design of potential vaccine candidates

Vaccine candidates are screened in animals to determine if they are safe, elicit immune responses and show protection in these animals

The process for manufacturing a vaccine must be reliable and practical. Ideally, it will also be inexpensive

Phase I and II safety and immunogenicity trials test if the vaccine candidate elicits immune responses

Phase IIb and III efficacy trials test if the vaccine candidate is protective

Regulatory authorities license the vaccine after reviewing trial results, allowing its introduction (*vaccine debut*) for public use

Surveillance conducted after licensure to ensure the continued safety of the vaccine

Planning, Coordination and Evaluation

Adapted from Ann McDonald-Cacho.Kahn, P. and L. Long. The immune system in pictures. In Kahn, Patricia, ed. *AIDS Vaccine Handbook: Global Perspectives*. New York. AIDS Vaccine Coalition. 2005. p. 36.

Discovery and Social Research ($22 M over 5 years)

- **Purpose: To strengthen research and research capacity focused on: discovery of HIV vaccines and related research (such as immune correlates, innate and adaptive immunity, T and B cell responses, antigens, adjuvants, vectors, etc.); and social, behavioural and ethical issues in HIV vaccines.**

- **Objectives:**
  - Create internationally recognized teams of Canadian and LMIC researchers.
  - Support individual or small teams of Canadian investigators in their efforts to contribute important knowledge to the global search for HIV vaccines.
  - Build capacity for HIV vaccines research in Canada and LMICs.
  - Create mechanisms for CHVI investigators and teams to collaborate with one another and other relevant international networks and consortia.

Clinical Trial Capacity Building and Networks ($16M over 5 years)

- **Purpose: To fill a globally recognized gap in HIV vaccine clinical trial capacity as identified by the Global HIV Vaccine Enterprise, particularly in LMICs where trials are ongoing or planned; and build on the Global Health Research Initiative (GHRI) Canada-Africa HIV Prevention Trials Capacity Building program. This component does not aim to support HIV prevention clinical trials themselves.**

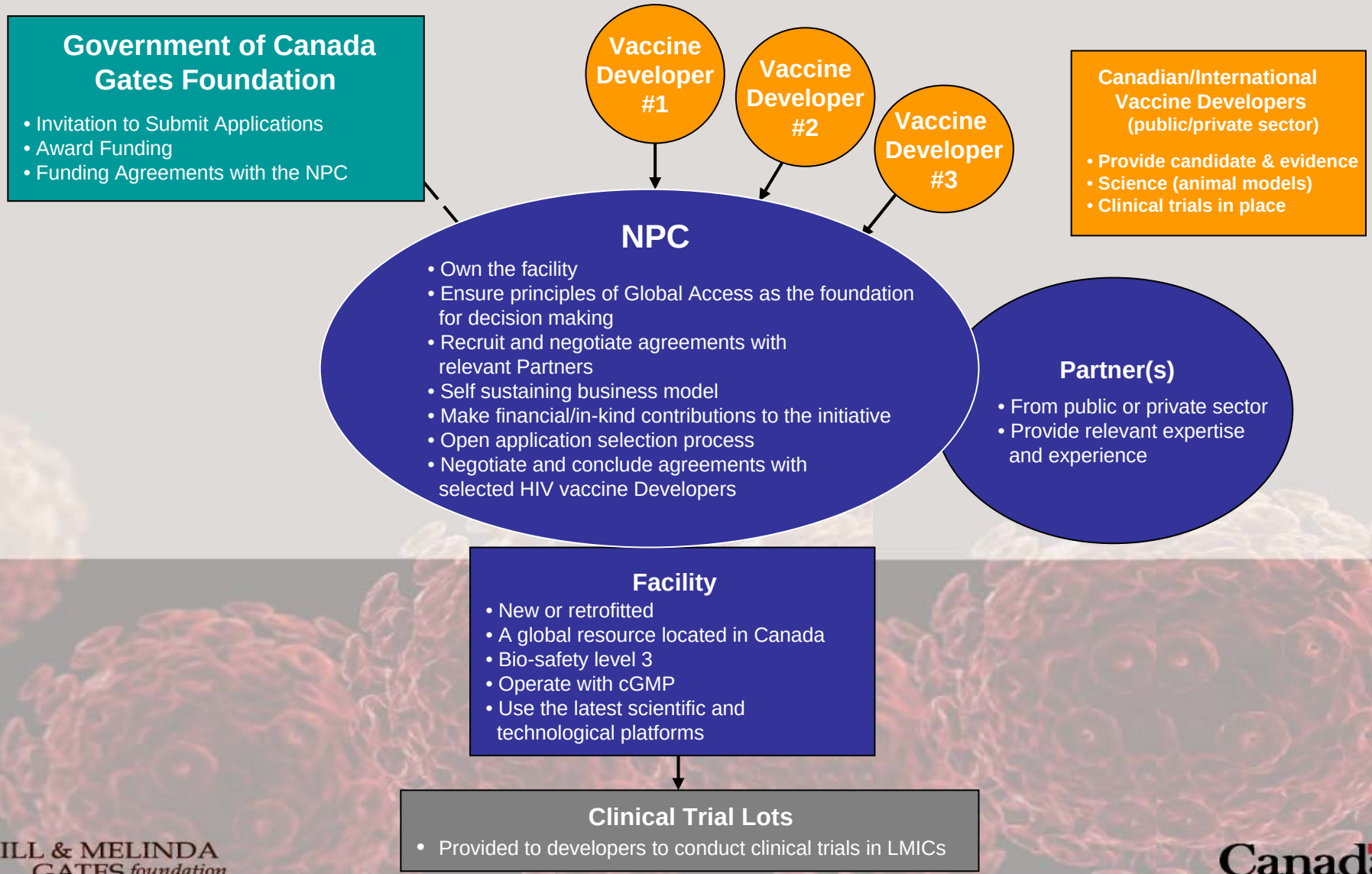
- **Objectives:**
  - To strengthen individual and institutional capacity in LMICs for the conduct of clinical trials related to new innovations in HIV prevention, particularly HIV vaccines.
  - To support partnerships (new or established) between Canadian and LMIC researchers and research institutions.
  - To support collaboration and networking, and increase involvement of Canadian and LMIC researchers and institutions in global HIV vaccine clinical trials efforts.

Pilot Scale Manufacturing Capacity for Clinical Trial Lots ($89M over 5 years)

- **Purpose: To address a global shortage in manufacturing capacity for clinical trial lots for promising HIV vaccines.**

- **Objective:** To establish a dedicated pilot scale manufacturing facility in Canada to produce HIV vaccine candidates for use in Phases I, II, III clinical trials, to be conducted mostly in and for the benefit of LMICs. The facility will be operated by a not for profit corporation (with private sector and other) partners.

Manufacturing Facility



Policy, Regulatory, Community and Social Dimensions ($8.5M over 5 years)

- **Purpose: To address policy, regulatory, community and social dimensions related to the development of a safe, effective, affordable and globally accessible HIV vaccine.**

- **Objectives:**
  - to strengthen vaccine policy approaches that promote global access to HIV vaccines;
  - to collaborate with partners in Canada and in LMICs in advancing legal, ethical and human rights dimensions of HIV vaccines, research and development, delivery;
  - to strengthen existing mechanisms to support community involvement in vaccine research and development, clinical trials and activities related to public awareness and education; and
  - to strengthen the regulatory pathway and processes for HIV vaccines in LMICs.

Summary of Accomplishments (June 2007 – March 2009)

- Governance structures in place (Interdepartmental Committees, Secretariat)
- Announcement of the CHVI (Ministerial) Implementation Advisory Board and appointment of Mr. Michael Sabia as chair
- Domestic and international stakeholders engaged through face-to-face and web-based consultations
- Majority of funding opportunities in place: Discovery and Social Research Operating Grants, DSR Catalyst Grants, Pilot Scale Manufacturing, Community Initiatives fund
- CHVI website in place (www.chvi-icvv.gc.ca)

Key Activities (2009-10)

- Awarding of funding to successful applicants for ongoing CHVI funding opportunities and launching of new funding opportunities (DSR Emerging & Large Team Grants, Clinical Trial Capacity Building and Networks via IDRC)
- Appointment of remaining CHVI Implementation Advisory Board members
- Completing consultations on a Policy Agenda for the CHVI
- Release of 1st Annual Report for the CHVI & Development of 2nd Annual Report
- Conduct Mid-Term Evaluation Study
- Launching of Communications Strategy
- Ongoing networking and partnership development opportunities

Section IV: Regulatory Affairs

Global Scientific Strategic Plan

- Many developing countries lack expertise and well-defined processes for reviewing and approving clinical trials and assessing results—a critical roadblock for HIV vaccine research, given that many trials will need to be conducted in developing countries.

- Priorities for action:
  - harmonize data/information needs across regulatory bodies;
  - facilitate regulatory decision making possibly using regional approaches for conducting reviews;
  - build regulatory capacity in developing countries;
  - identify and remove potential scientific impediments to rapid regulatory decision making, and
  - address ethical issues that interface with regulatory decision making, such as ensuring informed consent and defining the degree to which trial participants should receive a standard of care that is higher than others in their community.

CHVI Regulatory Affairs activities

- CHVI Objectives
  - Strengthening the regulatory pathway and processes for HIV vaccines in LMICs
  - Strengthening vaccine policy approaches that promote global access to HIV vaccines.

- Activity #1: Strengthening NRA Regulatory Capacity in Africa ($2M over 4 years)
  - Focus on training opportunities & exchange of personnel, information sharing, cooperation in policy and regulatory framework development, and promoting and facilitating regulatory harmonization.

- Activity #2: Addressing key policy barriers
  - International consultations are underway to identify current policy barriers and those barriers where Canada can make a significant contribution to global efforts <Consensus to date -- regulatory policy barriers should be considered by Canada>

Health Canada Regulatory Affairs Activities

- Health Canada's Biologics and Genetic Therapies Directorate has actively participated in AVAREF (African Vaccine Regulatory Forum) since 2007
  - Established by the WHO to strengthen and build capacity for National Regulatory Agencies in African countries in which clinical trials for HIV are currently ongoing.
  - Includes representatives from African NRAs and regulators from developed countries.
- BGTD actively involved in AVAREF working groups
  - Task Group on Harmonization of Regulation of Clinical Trials of Medicines and Vaccines
- BGTD is exploring designation as a WHO Collaborating Centre on Biologic Standardization.

AVAREF Task Group: Harmonization of regulation of clinical trials of medicines and vaccines

- Identify types of capacity building activities that should be done in common for drug and vaccine trials
- Propose a list of required training and tentative timelines.
- Identify key elements to optimize the use of resources at the national level for the oversight of clinical trials of drugs and vaccines
- Identify the advantages/disadvantages of harmonized regulatory guidance documents for all processes relevant to oversight of clinical trials
- Prepare a list of documents that can be proposed for common use in the region
- Propose a plan for optimization of resources in the region with regards to evaluation of clinical trial applications and inspections

Moving Forward on Regulatory Affairs: A Collaborative Approach

- CHVI and BGTD will share expertise, resources and networks to advance common objectives related to strengthening global regulatory capacity, with a focus on low-and-middle income countries.

- CHVI and BGTD will be working closely with WHO, Global HIV Vaccine Enterprise, developing country NRAs, FDA, EMEA, scientists, advocates and others through a new proposed Global Regulatory Forum for HIV vaccines and other related health products

Moving Forward (cont'd)

- Proposed Global Regulatory Forum
  - Vehicle to set global priorities for action, mobilize expertise and resources as well as promoting new innovations and collaborations.
  - Co-led by CHVI-BGTD and WHO, in partnership with the Global HIV Vaccine Enterprise.
  - Made up of developing and developed country NRAs as well as representatives of key global HIV vaccines developers and advocates, and other funding partners.
  - The first Forum is planned for late 2009/early 2010.
  - A planning committee will be struck in Spring 2009.

Acknowledgements

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- Other CHVI Participating Departments and Agencies (Canadian International Development Agency, Industry Canada, Canadian Institutes of Health Research, Health Canada)
- Kwasi Nyarko, Biologics and Genetic Therapies Directorate, Health Canada
- Alan Bernstein, Global HIV Vaccine Enterprise

For more information:

Canadian HIV Vaccine Initiative

www.chvi-icvv.gc.ca

www.icvv-chvi.gc.ca

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