

# CHALLENGES FOR INTELLECTUAL PROPERTY MANAGEMENT OF HIV VACCINE-RELATED RESEARCH AND DEVELOPMENT: PART 2, THE CANADIAN CONTEXT

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On 20 February 2007, Prime Minister Stephen Harper announced a commitment by the Government of Canada and the Bill & Melinda Gates Foundation to fund and support the Canadian HIV Vaccine Initiative (CHVI),<sup>1</sup> an effort to accelerate the development of an HIV/AIDS vaccine and address critical research gaps identified by the Global HIV/AIDS Vaccine Enterprise (GHAVE).<sup>2</sup> The goal of the CHVI is to coordinate research within Canada as well as Canadian contributions to the international efforts to develop safe, effective, affordable, and globally accessible vaccines.<sup>3</sup>

Canada's commitment to HIV vaccine research is longstanding. In 2002, Canada promised at the XIV International AIDS Conference, held in Barcelona, to develop a Canadian HIV/AIDS vaccine plan focusing "on vaccine production and equitable distribution...this plan will support the global vaccine effort and will contribute to a better understanding of the complex legal, ethical and human rights issues involved in addressing access to vaccines

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1 The CHVI is a collaborative undertaking between the Government of Canada (Canadian International Development Agency, Public Health Agency of Canada, Industry Canada, Canadian Institutes of Health Research, Health Canada) and the Bill & Melinda Gates Foundation.

2 Office of the Prime Minister, News Release, "Canada's New Government and Gates Foundation announce support for HIV/AIDS vaccine research" (20 February 2007), online: Office of the Prime Minister <<http://pm.gc.ca/eng/media.asp?id=1544>>.

3 Canadian HIV Vaccine Initiative (CHVI), "Goals," online: CHVI <<http://www.chvi-icvv.gc.ca/goal-objec-eng.html>>.

and treatments for people living with HIV/AIDS, nationally and globally.”<sup>4</sup> The *Canadian HIV Vaccines Plan: Towards a World Without AIDS* was published in 2006,<sup>5</sup> and calls for Canada to contribute towards

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 diplomacy; and a strong health care ... system.<sup>6</sup>

To accomplish these goals, it is necessary to ascertain and respond to the key non-science challenges to HIV vaccine research in Canada, focusing on any potential intellectual property (IP) bottlenecks. This paper builds upon the key issues identified in Part One of this series of two papers on “Challenges for Intellectual Property Management of HIV Vaccine-Related Research and Development” [hereinafter, Part One]. Following that review of the global literature and consultations with international experts,<sup>7</sup> we consulted with representatives from the CHVI and developed sector-specific interview guides for academic researchers, government, and industry representatives in Canada. We conducted individual or group interviews with 21 key informants in Canada, including CHVI representatives, experts in intellectual property law, management and ethics, as well as academic and pri-

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4 Paul Gully, “Address” (Remarks presented to the XIV International AIDS Conference, Barcelona, Spain, 5 July 2002) [unpublished]; R. Elliott *et al.*, *Putting Third First: Vaccines, Access to Treatment & the Law* (Montreal: Canadian HIV/AIDS Legal Network, 2002) online: INFO Project <<http://www.popline.org/docs/276662>>

5 Public Health Agency of Canada (PHAC), *The Canadian HIV Vaccines Plan: Towards a World Without AIDS* (Ottawa: Canadian Public Health Association, 2006), online: Public Health Agency of Canada. <[http://www.phac-aspc.gc.ca/aids-sida/pdf/publications/vaccplan\\_e.pdf](http://www.phac-aspc.gc.ca/aids-sida/pdf/publications/vaccplan_e.pdf)>.

6 *Ibid.*

7 See Lori Knowles & Tania Bubela, “Challenges for Intellectual Property Management of HIV Vaccine-Related Research and Development: Part 1, the Global Context” *Health L.J.* (2008) 16 *HealthL.J.* 55.

vate sector HIV vaccine researchers.<sup>8</sup> Here, we present the conclusions from those interviews, a discussion of key concerns, and potential solutions.

The consultations focused on the main non-science barriers to HIV vaccines (R&D) in Canada. The main challenges identified from a research perspective surprisingly did not include issues related to IP, but were, instead, inadequate funding for research, clinical trials and gap funding for taking innovative research to the proof of principle stage. There are also problems associated with the creation of effective research networks and collaborative models. Further downstream, there will be major challenges associated with manufacturing and distributing vaccines, particularly in developing countries, and the associated risks of liability for adverse events, such as allergic reactions to the vaccine. This latter issue has already come to the fore in HIV vaccine clinical trials known as the Step Study. The vaccine, manufactured by Merck and Co., was found to increase the susceptibility of participants to HIV infection if they had high levels of antibodies to adenovirus 5. Adenovirus 5 was a component of the vaccine and is one of the causes of the common cold. Indeed, an independent Data and Safety Monitoring Board went so far as to recommend unblinding the results and notifying participants whether they received the Merck vaccine or the placebo.

However, we were specifically interested in potential challenges for Canadian researchers and HIV vaccine development posed by (IPRs) in the HIV vaccine space. As outlined in Part One of this series, those challenges include the potential for a patent thicket whereby a plethora of patents on essential vaccine components and processes held by a variety of entities will make it virtually impossible to negotiate all of the licenses necessary to manufacture and deliver an HIV vaccine. We therefore asked a series of questions related to IP management (Appendix One). When probed, interviewees suggested that Material Transfer Agreements (MTAs), the licenses for use whereby tools and materials necessary for research are transferred between researchers or institutions, were a greater hindrance to vaccine research in Canada than were patents per se. This is in accordance with surveys of researchers in a range of life sciences disciplines conducted in the United States, where most researchers operate under the assumption that their research activities will not trigger a patent infringement suit – not because there is, in fact, a statutory or common law research exemption, but because the adverse

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8 Key informants were guaranteed anonymity so that they could be frank with their comments. Thus, quotes are not attributed with any identifiers.

publicity and cost of such a suit make it unlikely that a patent holder would assert its rights against a public sector researcher. Instead, access to materials required for research may be denied for practical reasons (e.g., the cost, labour and time involved in shipping samples), because of old fashioned competition between researchers, and because university technology transfer offices have inserted overly complex terms into MTAs, based on unrealistic expectations of returns to the institution or potential liabilities.

In relation to experienced or potential IP roadblocks as HIV vaccine R&D advances in Canada, we then asked interviewees from each sector – academia, government, industry – about their respective roles in avoiding and/or overcoming patent-related roadblocks, potential models for enhancing collaboration between public sector researchers and industry, and how best to align Canadian policies with those being developed internationally to enhance HIV vaccine R&D and ensure global access to its products and processes. What follows is a summary of the key issues and potential solutions raised during our consultations.

## **Main Non-Science Barriers to HIV Vaccines Research and Development in Canada**

According to key stakeholders, the main non-science challenges to HIV vaccines R&D in Canada are funding, creating effective networks and collaborative models, future manufacturing and distribution strategies, managing liability and the risks of adverse events, and managing expectations. Interestingly, only a few interviewees identified IP issues as significant barriers to HIV vaccines R&D.

Ironically, IP issues may prove to be a barrier inversely to the way originally anticipated. Rather than widely dispersed and prevalent IP posing a barrier to HIV vaccines research, the *lack* of IP barriers is indicative of the inadequacy of funding and investment to support HIV vaccine R&D. As one interviewee noted, the nature of the potential market for HIV vaccines (i.e., primarily populations in low- and middle-income countries) may explain why IP issues are not one of the key barriers: *“If it was highly lucrative for the private sector, there’d be much more exclusivity.”* Specifically, interviewees noted that meeting the scientific challenges of HIV vaccines research requires more funding than is typically available through public funding, and without IP as an incentive, pharmaceutical companies are unlikely to invest in HIV vaccines R&D. They also felt that a major barrier to industry involvement in HIV vaccines R&D is a perceived lack of return on investment. Government representatives were also not able to identify specific IP bottlenecks, but they

did feel that their respective departments had a role in alleviating any such barriers.

The lack of IP barriers may, in part, be the result of the close-knit nature of the Canadian HIV vaccine research community, which is relatively small and therefore researchers know each other quite well. One interviewee noted that licensing of IP is useful for sharing information between people who don't know each other, but in a closely knit research community, licensing is just a formality for conduct that happens anyway. Thus, IP issues were not identified as the main barrier to HIV vaccines research collaboration in Canada.

## Funding

There was consensus among the interviewees that funding is the main challenge for HIV vaccine researchers in Canada, falling into four distinct categories: academic research funding, clinical trial funding, investment in early-stage companies, and venture capital.<sup>9</sup>

### *Academic Research*

There was consensus that academic researchers in HIV vaccines R&D require more funding than is typically available through public agencies. Public funds are relatively small in Canada, requiring investigators to apply frequently, creating fatigue amongst researchers. Many of the interviewees called on the Canadian Institutes of Health Research (CIHR) to continue to fund HIV vaccines R&D, both within Canada and through contributions to global initiatives such as the CHVI. This CIHR funding, according to interviewees, should be provided according to priority areas identified by scientific experts, balancing support of new innovations with targeted research programs for promising approaches. Some of the interviewees felt that Canada is in a good position to contribute to HIV vaccines R&D, through its *"good labs and science."*

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9 See Canadian HIV Vaccine Initiative (CHVI), "Consultation on Canadian HIV Vaccine Initiative (CHVI) Funding Programs," online: CHVI <<http://www.chvi-icvv.gc.ca/fund/index-eng.html>> (this message was heard at a consultation on the CHVI funding programs from domestic and international stakeholders, and will inform the development of the CHVI's Request for Proposals/Application).

One informant was a proponent of the Gates Foundation's Grand Challenges approach, which proactively defines research priorities. Under this model, Canada's research funding would be distributed through Requests for Applications (RFAs) in priority research areas, providing coordinating mechanisms and personnel to manage the overall research program.

While CIHR reported that it could play a key role in accelerating HIV vaccines research by offering targeted research programs (e.g., under the CHVI<sup>10</sup>), some interviewees noted a preference for freedom to pursue creative and innovative ideas through investigator-initiated research grants, enabling riskier research that *"does not fit the mould."*<sup>11</sup> They were disappointed with previous models that used the targeted funding approach, finding that they stifled creativity.<sup>12</sup>

10 Funding under the CHVI is administered by the Canadian International Development Agency, the Public Health Agency of Canada, the Canadian Institutes of Health Research, Health Canada, and the Bill & Melinda Gates Foundation in four key areas: Discovery and Social Research (\$ 22 mill.), Clinical Trial Capacity Building and Networks (\$16 mill.), Pilot Scale Manufacturing Capacity for HIV Vaccine Clinical Trial Lots (\$89.1 mill.), Policy and Regulatory Issues, Community and Social Dimensions (\$8.5 mill.). A further \$3.4 mill. is earmarked for planning, co-ordination and evaluation. See Canadian HIV Vaccine Initiative (CHVI), "Funding Opportunities," online: CHVI <<http://www.chvi-icvv.gc.ca/fund-eng.html>>.

11 *"In many instances, grant review committees are made up of old timers in the field who are set in their ways and with ideas carved in stone. So truly innovative research that does not fit the mould gets slowed down because it doesn't get funded. For vaccine development there is a need to take a certain amount of risks and pursue avenues that are non-traditional – approaches that move outside the box. Researchers want to attempt these truly innovative experiments and take approaches outside the box, but these may not score well in the peer review process... We also need further investment in modeling. We have to be more open to invest out of the box in experiments and approaches to shed light on questions, at least go to the proof of concept stage that may be built upon."*

12 *"I was disappointed with [CANVAC - the Canadian Network for Vaccines and Immunotherapeutics] because, well, part of the problem was that it was largely focused on products and strategies quite far down the pipeline and in Canada we just aren't that advanced in the HIV field. But lots of great ideas and talented researchers that were working on ideas in early phases, were really hobbled because the focused RFAs keep researchers focused on ideas that are not their own. Unless we allow investigators to focus on their strengths, we just can't be that competitive internationally... And that's always one of the criticisms of having this type of funding provided through RFAs as opposed to investigator-initiated*

In addition, the scientific challenges of HIV vaccines research require “a critical mass of manpower to work on certain questions,” and “[t]here are not enough researchers working on it, not enough funding in the field, and whatever funding is available is too fragmented.” Thus more funding is needed – in particular, salary support for researchers.<sup>13</sup> All informants felt that significant funding is needed to attract researchers to focus on HIV vaccines.

### *Clinical Trials*

Interviewees explained that HIV vaccine research projects often get stalled at various stages along the research continuum due to the piecemeal nature of funding. Projects may stall at the basic science phase or animal model trials because researchers don’t have the resources to conduct human proof of principle and toxicology studies. Once that stage is achieved, the technical risk is reduced and private shareholders may be more interested in supporting later stage clinical trials. Pre-clinical researchers (both academic and private sector) often face significant hurdles in moving their projects to clinical trial phases due to uncertainty about whether success in animal models is indicative of success in humans, and thus experience difficulty raising funds to proceed with the research.<sup>14</sup> Before clinical trials can commence, researchers need to scale up their candidate to clinical lots, ensuring good manufacturing practice (GMP) for human trials – an expensive stage. Clinical trials in humans require infrastructure akin to full manufacturing processes, and there are no funding bodies in the range of \$200,000 to \$1 million to produce a clinical lot for clinical trials. The HIV Vaccine Trials

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*research. You don’t actually get novel ideas coming out because they just don’t fit the funding for the ideas of the people writing up the RFAs, so it’s hard to be creative.”*

13 The CIHR has recommended investment in salary support programs for researchers. See Canadian Institutes of Health Research (CIHR), *Task Force on Career Support: Final Report* (Ottawa: Canadian Institutes of Health Research, 2004), online: CIHR <[http://www.cihr-irsc.gc.ca/e/documents/re\\_taskforcereport\\_e.pdf](http://www.cihr-irsc.gc.ca/e/documents/re_taskforcereport_e.pdf)>.

14 *“Ironically, we started this company because we thought it would be easier to get the financing as a company and not as academics (this was pre-Gates). We thought there would be more funding from private sources but ultimately this proved to be incorrect. There is limited private money going into HIV vaccine research...Only big pharma manages to advance its programs for a variety of reasons, including political/philanthropic imperatives, credibility and track record in bringing successful products, including vaccines, to market. This allows them to attract public funding (whether through academic partners, or not) to help share in the burden.”*

Network (HVTN) in the US was suggested as a model which provides the infrastructure necessary to manufacture vaccine candidates and test them in humans. Further funding is then needed to run various stages of clinical trials, particularly phase two trials, which require international participation, significant investment and perhaps assistance from private-public partnerships (PPPs) (e.g., the International AIDS Vaccine Initiative or the HVTN), governments and NGOs in building trial infrastructure in developing countries.

### ***Gap Period Funding***

According to an IP expert, a big challenge in Canada is in early funding for what is known as the “gap period.” In Canada, one of the most effective ways to transfer technology is to create spin-off corporations or to license companies with vaccine portfolios. The “gap” is in funding to take research projects from innovative ideas to proof of principle stages.<sup>15</sup> Technology Transfer Offices (TTOs) identify the lack of funding for the “gap period” as the number one challenge facing Canadian innovation.<sup>16</sup> According to one interviewee, biotechnology companies which are not affiliated with any academic institution “*try to do the right thing*” by acting independently, with only private sources of funding (rather than tapping into limited public funds). Industry informants explained the difficulty in attracting financing for HIV research programs; other areas of vaccine research (e.g., influenza) more easily attract investments because there is more room for new innovation. Companies can more easily demonstrate substantial improvement over the currently available vaccines, and therefore attract investment, when there are many vaccines on the market to compare to. This is not the case with HIV vaccine research, where requests for industry support receive responses such as: “*Even if I believe that what you have will work, there is nothing for me to*

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15 The CIHR's Corporate Commercialization and Innovation Strategy is designed to address this gap by awarding grants to researchers at academic institutions and research hospitals to conduct 12-month proof of principle studies. The grants are provided in two phases – phase one (up to \$150,000) is provided when the IP still resides with the academic researchers, and phase two (up to \$250,000) is provided once a partnership is established with a private sector partner. At this stage the IP is often, but not necessarily, licensed to the private sector partner.

16 Centre for Intellectual Property Policy (CIPP), *Technology Transfer Workshop Issue Paper* (Montreal: Centre for Intellectual Property Policy, 2004), online: CIPP <<http://www.cipp.mcgill.ca/data/publications/00000005.pdf>>.



*compare it to – there is no measure of success. I can't say that what we are seeing in monkeys, for example, is indicative of success in humans.*" One of the industry informants explained that only angel investors<sup>17</sup> tend to be willing to finance new start-up companies doing HIV vaccines research.

### ***Venture Capital***

Other challenges relate to financing a candidate product all the way to a marketable product. Canada, unlike the United States, does not have well developed venture capital around biotechnology. Canada sometimes loses IP to the US because of the lack of venture capital in the biotechnology field.

Overall, interviewees called upon the government to identify critical "gap period" funding needs, identify research areas where risks are greatest for researchers and investors, and strategically focus funding to mitigate those risks.<sup>18</sup> Some interviewees encouraged funders to focus on PPP mechanisms to leverage government funds along with NGO funds, private sector investments, and funding from other levels of government *"to better align activity and have all oars pulling in the same direction."* Another interviewee encouraged funders to take a long-term view, given the lengthy period required for HIV vaccines R&D, and cautioned that *"throwing a lot of money in won't necessarily speed things up, but the money needs to be focused and targeted."*

17 An angel investor (known as a "business angel" in Europe) is an affluent individual who provides capital for a business start-up, usually in exchange for convertible debt or ownership equity. A small but increasing number of angel investors are organizing themselves into angel networks or angel groups to share research and pool their investment capital. See Center for Venture Research, "CVR News," online: Whittmore School of Business & Economics University of New Hampshire <[http://wsbe.unh.edu/Centers\\_CVR/2006pressrelease.cfm](http://wsbe.unh.edu/Centers_CVR/2006pressrelease.cfm)>.

18 The Government of Canada launched in June 2007 a national competition for the creation of 10 Centres of Excellence in Commercialization and Research (CECR). One meeting (May 2007), hosted by the University of Toronto, McLaughlin-Rotman Centre, Program on Life Sciences and Global Health, successfully brought 30 companies from developing countries to Toronto to meet with Canadian venture capitalists companies to discuss neglected diseases and R&D issues. The Centre is planning to hold more such workshops, and will be applying for CECR funding to train venture capital to focus on commercializing Canadian life sciences research in emerging and developing country markets.

## Creating Effective Networks and Collaborative Models

Another key challenge is creating the leadership and funding to have researchers (particularly those in academic settings) work together and build a “critical mass” for pursuing any one line of enquiry. Academic researchers are more accustomed to pursuing investigator-driven research which on one hand is important for innovation and creative ideas, but on the other hand makes it difficult to comprehensively tackle complex candidate vaccine concepts. A common sentiment of the interviewees was: “*No one is going to come up with an HIV vaccine by working in isolation in their own lab.*” Different research and institutional cultures in the HIV vaccines research sector present a barrier to national and international institutional collaboration and coordination.<sup>19</sup>

There are a number of challenges in vaccines research in general that also apply to HIV vaccines research. One researcher noted that one of the challenges in partnerships between academic researchers and industrial partners is that the companies tend to have their own business plans and agendas which co-opt the academic researchers’ interests. One interviewee, for example, described a promising project that was to be co-sponsored by public and private sector supporters. While a significant amount of time and energy was spent in developing the partnerships and the research proposals, the industry partner ultimately decided against the investment: “[*the company*] stopped the project because they had other fiscal motives. And we were stuck because it was [*the company’s*] compounds that we were working with.”

One of the IP experts cited a consultation his group conducted with biotechnology companies in Canada, to determine if they had products relevant to the developing world, how prepared they were to move forward, and what obstacles they were encountering. The first obstacle identified was financing, particularly for clinical trials in developing countries. The second obstacle was the ability to identify and pre-qualify potential local partners. Some Canadian companies reported that they do not know how to approach

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19 “How can researchers within different systems and different systems of accreditation and merit find a common language to allow for the level of collaboration that needs to take place in this type of research endeavour? How do we get researchers to speak together? Here in the HIV context we see groups like agencies and research institutes and hybrid institutions taking a lead role... The institutional context is often ignored but needs to be considered and is of growing importance with hybrid institutions involved in these research endeavors.”

developing country partners, and felt that the Government of Canada is not doing enough to facilitate linkages and partnerships with developing country partners. Developing country researchers are members of many consortia but are rarely senior or principal investigators, with the possible exception of South Africa. However, research consortia are shifting away from North-led and -imposed R&D to a more local and South-led and -driven approach. HIV vaccines R&D capacity is increasing in developing countries beyond South Africa, notably in Botswana, Tanzania, Kenya, Uganda, Rwanda, Zambia, Nigeria, Cameroon and Senegal. Building capacity of developing countries in the full spectrum of HIV vaccines R&D, from discovery to clinical trials, is an important step to accelerating access to vaccines in the countries hardest hit by the HIV pandemic. It is important to note that level of capacity varies amongst developing countries, with some already having advanced capacity and other countries which would benefit from capacity building in specific areas or activities.

### Future Manufacturing and Distribution Strategies

Another major non-science barrier to HIV vaccines R&D is the future cost of vaccines, once they are developed. Cost for vaccine doses will vary depending on whether the vaccines are to be administered therapeutically or preventatively, on the nature of the delivery method, and on when and how frequently the vaccine will need to be administered, as well as to whom.

One IP expert explained that vaccine research is currently supported through two predominant models: 1) through major national programs of research funded by national governments or private foundations (e.g., Gates Foundation's Grand Challenges Initiative); and 2) through a variety of product development PPPs, also involving significant funding from private foundations such as the Gates Foundation. Many of these initiatives will reach the stage of producing a viable vaccine candidate, but delivering the vaccine to people requires prioritization with respect to which vaccine to use, when and where. Thus, a major hurdle will be with respect to who will make these prioritization decisions. At present, GHAVE has taken the steward role for global HIV vaccine R&D efforts, and is considered a legitimate, independent body to decide quality and delivery issues.<sup>20</sup>

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20 One of the interview informants recommended that the World Bank/UNDP/ UNICEF/WHO Special Programme for Research and Training in Tropical Diseases (TDR) could also adopt such a stewardship role. TDR could potentially

### Managing Risk of Adverse Effects

Some of the interviewees noted that many interesting and novel approaches to HIV vaccine research do not receive funding because they would not be licensable in Canada (by Health Canada) or in the US (by the Food and Drug Administration), even if those vaccine candidates would be very beneficial in high-prevalence settings such as sub-Saharan Africa. One of the interviewees recommended that funding programs and regulators should consider the target population of the vaccine concepts (e.g., low prevalence versus high prevalence settings), assessing the risk-benefit ratio relative to the number of infections that will be prevented.<sup>21</sup> While ideally the hope is to develop the best possible vaccine, and to prioritize and apply uniformly safety standards across all countries, pragmatically, the risk-benefit standard may be adjusted based on the actual risk in the context in which the vaccine is being used.<sup>22</sup>

### Managing Expectations

Finally, according to one prominent HIV vaccine researcher, the main non-science barriers of HIV vaccines research are: managing expectations, taking into account challenges around global access, capacity building, how to measure success and how the level of success varies between the developed world and the developing world, and how to communicate all these complexities to multiple stakeholders.

### Lessons Learned from the Previous CANVAC Model

Many of the informants emphasized the need in Canada for a model of collaboration between the pharmaceutical industry, researchers, government and community-based organizations, building on lessons learned from the

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facilitate research networks across areas of neglected diseases affecting developing countries, and take on the role of deciding the appropriate interventions, where to use interventions, at what stage, and with what provisos.

21 For example, in Canada, 1 in 10,000 adverse effects is not acceptable, but in high prevalence regions, the benefit of a vaccine would be considered higher, even with a 1 in 10,000 adverse effect rate.

22 See Rotavirus example explained in *supra* note 7; see also Anthony D. So, Arti K. Rai, & Robert M. Cook-Deegan, *Intellectual Property Rights and Technology Transfer: Enabling Access for Developing Countries* (N.p.: Commission on Intellectual Property Rights, Innovation and Public Health, 2005).

Canadian Network for Vaccines and Immunotherapeutics (CANVAC).<sup>23</sup> CANVAC, which operated from 2000 to 2006, was formed because of the identified need for more sharing of information and less isolation, “*taking the approach that vaccines research together is better than separate.*” 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. Essentially, CANVAC aimed to play a matchmaker role between industry and academic research partners, particularly for therapeutic HIV vaccines. CANVAC also attempted to address the barrier of inadequate clinical infrastructure to develop clinical trial cohorts for vaccine R&D.

According to some of the interviewees, the general problem with CANVAC’s model was the difficulty in managing and coordinating the efforts of academic researchers to work together towards a goal or, in the case of HIV vaccines R&D, of developing three or four vaccine candidates. One of the researchers who was involved in CANVAC’s HIV vaccines development project found that “*it was like herding cats*” to try to coordinate the efforts of university researchers towards one candidate vaccine concept. The efforts of CANVAC to coordinate the research efforts of academic scientists were unsuccessful largely because university-based researchers prefer to operate under investigator-driven grants rather than be accountable for contributing to a pre-designated research goal. Some interviewees described CANVAC as operating from an industrial model. Researchers in the network were expected to complete specific projects with the CANVAC investments given to them, but CANVAC found that it was very difficult to make academic researchers accountable.<sup>24</sup>

Some of the interviewees felt that the CANVAC model – “*bringing together a bunch of scientists all over Canada where they would network and do team type*

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23 In June 2005, CANVAC learned that it did not have its funding renewed by the Natural Sciences and Engineering Research Council as a Network of Centres of Excellence.

24 One of the interviewees generally felt that there is low accountability from academic researchers for the funding that they receive: “*if they publish, they get more money, but they don’t have to necessarily publish on what they said they would do.*”

projects” – was promising, and that the government should have provided some assistance in managing the Network.<sup>25</sup> However, one of the researchers involved with the former CANVAC noted that the network didn’t hold any patents related to HIV vaccines, partly because of budgetary constraints (writing and filing a patent would cost at least \$20,000, in addition to annual fees) and partly because it was reluctant to align with one specific vaccine candidate.<sup>26</sup> Another disagreed, feeling that the network became overly embroiled in IP issues.<sup>27</sup>

The key lessons identified by interviewees to be learned from the CANVAC are that:

- 1) the “herding cats model” is not likely to produce an HIV vaccine in Canada;
- 2) more funding for researchers is necessary, as is more accountability for how that money is used; and
- 3) the full infrastructure (with basic science labs and clinical experts) is necessary for following a vaccine concept from its basic science stages through to clinical trials.

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25 See Laura Eggertson, “Vaccine network surprised by funding cut” (2005) 173 CMAJ 741 at 741 (“Even if the research is excellent, a network is more than just that,” says Nigel Lloyd, executive vice-president of NSERC. Network applicants are also judged on their ability to develop highly qualified personnel, establish partnerships, facilitate knowledge and technology transfer, and manage the network).

26 *“It’s a very busy field and it was difficult to really establish a clear patent position because there are so many ideas out there. CANVAC’s role was to try to develop a patent portfolio, with all the patents negotiated with universities which would hold the patents. The idea was that CANVAC would pay for the patent and try to bundle IP to try to attract investors, work with companies to try to get them to invest in Canada. CANVAC held IP only in immuno-modulation molecules, tools to enhance the immune response, which are applicable to many types of vaccines.”*

27 *“The intention of CANVAC was to partner with private companies, get a certain number of candidates into the pipeline, broker the IP issues, but then it got them interested in holding the IP. They should have been there to help researchers manage the IP issue but essentially what happened is that it got another agency interested in getting a piece of the IP since they funded the research, so they were all of a sudden fighting with both the university researchers and their industry partners. So researchers started to feel that this was too complicated.”*

Finally, CANVAC and the CIHR are based on virtual institutes, without any physical institution with labs and experts working in one place like the HVTN in the US.<sup>28</sup> Several interviewees recommended that Canada initiate and support a vaccine centre in a location attractive to researchers.<sup>29</sup>

## IP-related Roadblocks

Only a few of the interviewees reported any patent-related roadblocks as a limiting factor in their HIV vaccines research activities. In support of this finding, CIHR stated that it hasn't received any reports from the research community to indicate that IP issues are a major barrier to HIV vaccines research. Some interviewees noted that patents actually facilitate more open discussion of IP: "*As soon as things are patented, most people are very open to discussing what they've found, especially in HIV since it's such a hot area.*"

## Material Transfer Agreements

One area where there may be IP concern is with respect to physical or biological materials where the IP is controlled through MTAs that dictate the terms under which materials (patented or not) are provided to researchers for use or testing. This observation is in keeping with other surveys of researchers in the United States.<sup>30</sup> One of the leading researchers in the HIV

28 The HIV Vaccines Trial Network (HVTN) units are located at leading research institutions in 27 cities on four continents. Internationally renowned HIV vaccine and prevention researchers lead the units. The Network's headquarters are at the Fred Hutchinson Cancer Research Center in Seattle, Washington.

29 One model that provides a good example is the Dale and Betty Bumpers Vaccine Research Center (VRC) at the NIH which was established to facilitate research in vaccine development. The VRC is dedicated to improving global human health through the rigorous pursuit of effective vaccines for human diseases. Established by former President Bill Clinton as part of an initiative to develop an AIDS vaccine, the VRC is a unique venture within the NIH intramural research program. The building and its facilities are funded by NIH, with a mission to conduct research that facilitates the development of effective vaccines for human disease, primarily HIV. The VRC employs immunology and virology investigators, clinical trials specialists, production and manufacturing specialists, and regulatory affairs specialists: "*the beauty of it is that the people that work there don't have to write grants because they're funded internally.*"

30 Timothy Caulfield *et al.*, "Evidence and anecdotes: an analysis of human gene patenting controversies" (2006) 24 *Nature Biotechnology* 1091; Wesley Cohen,

vaccines field reported that MTAs are the primary mechanism for handling IP transfers and are useful in clarifying rights in collaborations such as co-authorship.<sup>31</sup> However, MTAs can present roadblocks to research because of restrictions placed on use,<sup>32</sup> especially at the clinical stage of research and with industry involvement.<sup>33</sup> There is also a concern about increasing levels of secrecy fueled by IP issues and a growing trend towards exclusivity.<sup>34</sup>

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Richard Florida & Richard Goe, *University-industry research centers in the United States: final report to the Ford Foundation* (Pittsburgh: H. John Heinz III School of Public Policy and Management, Center for Economic Development, 1994); John P. Walsh & Wei Hong, "Secrecy is increasing in step with competition" (2003) 422 *Nature* 801.

- 31 "I've never turned anybody down when they request an MTA. Actually, I'm careful to use MTAs rather than just informally send them on even though I want to be collegial. It's extra work to go through the formal MTA process, but it helps with keeping up your own stock. The hard part is knowing at what point do you get considered as a co-author? Delineating what is just a material transfer versus a collaboration is tricky. We write up MTAs but we never write up a collaboration agreement – we probably should. As I've had more and more post-hoc squabbles, I've tried to be more upfront verbally on authorship issues, particularly if we spend a lot of time and energy in getting the products ready for the partners."
- 32 "Had I waited to get patents negotiated to go forward, it would have been a huge roadblock, but my approach has been to ignore patents. We just use material transfer agreements from another academic who lets you use their compound to do your academic research, with restrictions not to patent it yourself or using it for commercial gain. But it can be very hard to get MTAs – because people at universities are protective, the institutions are very careful about not letting anyone in on the patent. There's a lot of research going on behind closed doors that is not being published until they're very far along because they're worried about getting their ideas scooped and losing the IP. We're not even allowed to present data at conferences because the IP lawyers are telling us to protect our IP until it's far enough along to be patented."
- 33 "Recently I requested research material from [name of university], and they said that it was licensed by a company and would be a headache to give it to me. There was another roadblock with a project when we were going to use a vector that was patented and licensed by another university and it would have cost us \$20,000 a year for that license and we just didn't have budget for that. When you get into the stage of clinical products, that's where you get into licensing difficulties."
- 34 "It's a detriment to the field; the willingness of researchers to make information available has been reduced in the last 15 years. In some ways, it makes it not a level playing field. There are the elite groups of labs - reagents and students and ideas flow nicely between



### Other Intellectual Property and Licensing Issues

IP issues may also become problematic in negotiating large R&D consortia and establishing the overall agreements between academic and private sector researchers to ensure access to background technology. These hurdles may be overcome through discussions, and the sense is they haven't presented any roadblocks to research progress. However, it was noted by an industry informant that there are problems with ascertaining potential patent roadblocks for IP arising from research consortia because it is difficult to fully predict the direction of research. There are also significant hurdles to patent searching to identify research project-related IP.<sup>35</sup>

In other areas of vaccine research, there have been concrete examples of patent-related roadblocks. For example, two separate Human Papillomavirus vaccines were developed by Merck and GSK, but both are excessively expensive for developing countries. With the pricing set in the north, these vaccines will never enter the healthcare systems of developing countries. While pricing is clearly an access issue, it could also be interpreted as a patent-related block insofar as cheaper generic pharmaceutical manufacturers are able (or not) to license the vaccines.

In other instances, it is not patents that are blocking access but trade secret protection:

*You don't necessarily need to patent the vaccine itself, it's the processes that go into making the vaccine that are trade secrets. For example, with the new Rotavirus vaccine, there two different vaccines made by two different processes, targeting the same disease. Having a patent won't prevent the competitors from designing a vaccine using a different strategy.*

In such instances, valuable resources may be wasted duplicating research efforts in developing an "invent-around."

Some of the interviewees did report IP-related roadblocks. According to one of the interviewees, IP is essential to attract industry funding; however, once obtained, an individual or an organization holding the IP rights may provide exclusive licenses which restrict access to essential components.<sup>36</sup>

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*them, but it's difficult for up and coming or smaller researchers to break into the field. You know, there are these invitation-only meetings, so it's becoming very elitist."*

35 See *supra* note 7 (for a discussion on issues about patent landscaping and due diligence).

36 "So it's really about accessibility to the component that you want to put in your vaccine

Researchers, including those in the private sector, can (and perhaps should) decide not to grant exclusive or co-exclusive licenses for their IP when being applied to HIV vaccines research.<sup>37</sup>

## Role of Stakeholders in Addressing Patent-Related Roadblocks

We asked the three groups of stakeholders – government representatives, academic researchers and industry – about their respective roles in avoiding and/or overcoming patent-related roadblocks.

### Government

There was general consensus that the most appropriate roles for government agencies were in providing funding, facilitating national and international networks of HIV vaccine researchers, encouraging increased industry participation and funding, and setting policies and guidelines for commercialization and IP arising from publicly funded research.<sup>38</sup> Interviewees acknowledged that political will and leadership are improving, with groups such as IAVI raising awareness and cooperation for clinical trials and private-public partnerships such as GHAVE and the Bill & Melinda Gates Foundation providing increased funding.

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*that's a very clear issue for any vaccine. Despite all the Gates money, a vaccine will not get developed because you won't get past that first step, it's all driven by people who hope to make profit. And making it attractive to industry requires putting a license on it or patenting it – it's essential. Nobody would touch it if there's no IP. And then once there is IP, you're going to get more money with more exclusive deals, and the more exclusive the deal, then of course...the more it restricts other people from using it. The trouble is, with HIV in particular, where probably a single thing won't work, you might need multi-component vaccines, then one person owns one part, another person owns another part, a third person owns a third part, and to get them all together and on the same page so that they can all be used together, is really tough because they've each got their own goals and they may not be matching."*

37 Coley Pharmaceutical Group, for example, has granted an exclusive license to Pfizer for the use of its CpG adjuvant for the purpose of cancer vaccine research, but any party may license the adjuvant for HIV vaccine applications. Also see Organisation for Economic Co-operation and Development (OECD), *Guidelines for the Licensing of Genetic Inventions* (Paris: OECD, 2006), online: OECD <[www.oecd.org/dataoecd/39/38/36198812.pdf](http://www.oecd.org/dataoecd/39/38/36198812.pdf)>[*Guidelines*].

38 *Ibid.*

### *Role of Funding Agencies*

Funding and coordinating agencies should follow the lead of the Bill & Melinda Gates Foundation in promoting policies aimed at Global Access and the NIH access policies more broadly.<sup>39</sup> Funding for the Grand Challenges funding initiative of the Gates Foundation requires a Global Access Strategy and annual reporting on progress in achieving the strategic goals.<sup>40</sup> The Gates Global Access Program also identifies ways in which technology can be made available at low cost for developing countries through innovative funding agreements and options such as differential pricing, etc. These funding models stretch the current Canadian policy norms. All of the respondents felt that the Gates Global Access Program appropriately balances global access “for those who need it most and can afford it least...recognizing that those who can should pay for it,” while ensuring adequate incentives for the private sector to participate in HIV vaccines R&D.

An important role for government (e.g., CIHR, Industry Canada), therefore, is to facilitate the development of IP policy guidelines for partnerships among and between academic and industry researchers, particularly with respect to the promotion of global open access to IP related to HIV vaccines research. The problem with the existing Tri-Council Guidelines<sup>41</sup> is that the

39 See *supra* note 7.

40 See Bill & Melinda Gates Foundation, “Annual Progress Report Guidelines – Grand Challenges,” online: Bill & Melinda Gates Foundation <[http://www.gatesfoundation.org/nr/Downloads/globalhealth/Grantseekers/GHGC\\_Annual\\_Report\\_Guidelines.doc](http://www.gatesfoundation.org/nr/Downloads/globalhealth/Grantseekers/GHGC_Annual_Report_Guidelines.doc)> at 8 (a questionnaire requires information on the membership of the collaboration, IP generated by the project, new proprietary background technology being used as a tool or incorporated into the innovation being developed, any trade secret protection, details of any agreements or rights on technology used or created by the funded project, results of any patent searching, any notifications that the use of any background technology may infringe another’s IP rights, and third-party technology of IP rights that could “(a) affect the freedom to practice or use the background technology or the ability to develop, make, use or sell any products intended to be developed through the project or (b) otherwise cause the use of the technology or product to infringe a third party’s rights?” In addition, a narrative summary is required of any issues that “could impact compliance with or furtherance of your Global Access Strategy”).

41 Adopted by the three primary Canadian funding councils – CIHR, National Sciences and Engineering Research Council (NSERC), and the Social Sciences and Humanities Research Council (SSHRC)

responsibility to exploit or to protect IP resulting from publicly funded research rests with researchers and their institutions. Since academic institutions across Canada do not have a harmonized IP policy,<sup>42</sup> there may be lack of clarity about who owns the IP across academic and industry collaborations.

However, the Tri-Council Guidelines also include a harmonized policy regarding the responsibility of researchers and institutions to ensure that the *maximum social and/or economic benefit is gained from publicly funded research*.<sup>43</sup> Although the language of the policy focuses on benefits to Canada and to Canadians, the CIHR interprets the policy to include issues such as HIV, which are globally relevant. This is a powerful statement which, if properly implemented, would allow the Canadian government to set policies to facilitate the goal of global access for HIV vaccine products and processes.

In terms of sharing the products and materials that may be patented, typically most organizations acknowledge that there is a period of time after discovery during which it is reasonable to withhold access or sharing of IP. CIHR's new policy on Access to Research Outputs<sup>44</sup> ensures access to results (publications and related data) of publicly-funded research,<sup>45</sup> but falls short of mandating the sharing of research materials and other non-publication related research data. An extension to the latter may be contemplated in the future, and would be in keeping with both CIHR's mandate and policy de-

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42 University IP policies vary by institution; IP may be inventor owned, or institutionally owned, or some combination. See Kate A. Hoye, *University Intellectual Property Policies and University-Industry Technology Transfer in Canada* (PhD Thesis, University of Waterloo, 2007) [unpublished].

43 Schedule 15 outlines the memorandum of understanding (MOU) that university institutions would sign prior to administering CIHR funding, which clearly outlines the CIHR's aim to maximize socioeconomic benefit to Canadians from the research results, IP protection as well as facilitating the transfer of IP to Canadian based entities, etc.

44 Canadian Institutes of Health Research, "Policy on Access to Research Outputs," online: CIHR <<http://www.cihr-irsc.gc.ca/e/34846.html>>.

45 U.S. Department of Health & Human Services, "NIH Data Sharing Policy and Implementation Guidance," online: U.S. Department of Health & Human Services <[http://grants.nih.gov/grants/policy/data\\_sharing/data\\_sharing\\_guidance.htm](http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm)>; Canadian Institutes of Health Research (CIHR), "CIHR Consultation: Developing a CIHR Access to Research Outputs Policy," online: CIHR <<http://www.cihr-irsc.gc.ca/e/33925.html>> ["CIHR Consultation"].

velopments at the NIH.<sup>46</sup> In consultations on the policy, conducted by CIHR, most researchers “felt that the requirement to share research materials and tools was acceptable and generally consistent with current research practice.”<sup>47</sup> If nothing else, these policies raise awareness of IP issues and of the fact that sharing data and materials is increasingly becoming good research practice.

In addition, funding agencies should play a leadership and co-ordination role in identifying IP generated using public funds, facilitating linkages and setting guidelines for research collaborations, and defining minimum expectations for the sharing of and eventual access to IP. Canadian funders should follow the lead of the NIH in setting creative licensing templates or guidelines to ensure access to developing countries.<sup>48</sup>

### *Other Roles for Government*

CHVI representatives explained that an important role for all government departments involved in the CHVI is to ensure policy coherence that would ensure that HIV vaccine R&D is accelerated and any resulting vaccine product is available quickly and at an affordable price. Government departments’ role is not only to provide funding to researchers and PPPs, but also to provide funding via the public healthcare system, to proactively develop policies regarding liability for the vaccine(s), to develop policies and procedures for roll-out of the vaccine(s), and to develop procedures for technology assessment.

46 See *supra* note 7; U.S. Department of Health & Human Services, “Principles and guidelines for recipients of NIH research grants and contracts on obtaining and disseminating biomedical research resources: final notice” (F.R. Doc. 99-33306) (Washington: Office of the Federal Register, National Archives and Records Administration, 1999), online: NIH Office of Technology Transfer <[http://www.ott.nih.gov/policy/rt\\_guide\\_final.html](http://www.ott.nih.gov/policy/rt_guide_final.html)>.

47 “CIHR Consultation,” *supra* note 45.

48 See *supra* note 7 (There are a number of creative licensing strategies used by both public sector and PPP groups to ensure that the benefits of health biotechnology reach the people in low and middle income countries. Humanitarian licensing strategies focus on avoiding future IP obstacles, with the goal of ensuring that people in the developing world get access to essential medicines. Most humanitarian licensing strategies are employed by universities when licensing IP to PPPs or to the private sector. These strategies can also be used by private philanthropy and by government funding agencies. The National Institutes of Health (NIH) in the United States engages in humanitarian licensing and has its own guidelines and policies for vaccines).

The government departments responsible for the CHVI were called on by interviewees to show leadership and commitment to aligning with the scientific strategic plan of the GHAVE, and to contributing in areas where Canada can have added value. Interviewees noted that government has a role in stimulating and supporting Canadian expertise from research to manufacturing, from policy to regulatory issues, particularly in ways that are different from the expertise provided by the US or by European countries. The end goal of all cohesive government policy should be for *“access to those who need it most – affordable, accessible – and understood by civil society what the limitations will be, and ensuring that there are no ethical mistakes along the way.”*

The Public Health Agency of Canada (PHAC) identified itself as playing a hands-on, central role in the CHVI, actively helping to steer and manage the Initiative. PHAC also identified ways in which it could apply leverage for accelerating HIV vaccines R&D, such as through its extramural research (in universities), in-house research (e.g., Micro Laboratory for the Ebola virus), and its responsibility for the National Immunization Strategy. PHAC makes scientific recommendations about to whom and when to administer vaccines. Finally, PHAC has taken a lead in the community involvement side of vaccines R&D, a role that they predict will be expanded upon. One of the interviewees from PHAC noted that community stakeholders are less interested in open access to IP of HIV vaccine research data, biomedical knowledge, or laboratory knowledge than they are in open access to the end products. PHAC sees itself playing a key role in engaging communities in discussions about the ultimate vision for access to HIV vaccines. A key PHAC role, therefore, is in supporting community education and community advisory boards (CABs) to become involved in directing HIV vaccines R&D, including addressing open science and open access issues.

The role of Industry Canada is to engage the private sector in the CHVI, particularly with respect to sharing private sector expertise in commercialization and manufacturing of products. Industry Canada, for example, could facilitate private sector involvement in the production of clinical trial lots, helping to ensure appropriate structures and policies that acknowledge the role of industry partners, facilitate greater linkages, and provide the industry perspectives on specific guidelines or licensing provisions. The Patent Policy Division at Industry Canada can assist in finding the balance between IP protection and financial incentives for the private sector.<sup>49</sup>

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49 *“We need to find a way to let a firm know that at the end of the day that they’ll be able*

## Industry

Interviewees noted that the private sector has had only limited involvement in vaccines R&D over the past twenty years,<sup>50</sup> although that interest is enhanced for products with market potential.<sup>51</sup> The main rationales for low industry investment are the poor return on investment from developing country markets, technical hurdles, and the risks involved in vaccine R&D and clinical trials and other liability issues.<sup>52</sup> That said, public sector research and funding “only gets vaccines to a certain point.” According to interviewees from the private sector, companies are very keen to partner with the public sector and academic researchers as a means of spreading out some of the science and non-science risks of vaccines R&D. Models such as the Advanced Market Commitment<sup>53</sup> pilot for pneumococcal vaccines, discussed below,

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*to make a return on their significant investments. If you take action that lessens that IP value, you're reducing some of the incentive, it drives the profit scale down, there's less potential for investment, and it all works against more innovation. At the same time, you need to balance against the public good. In Canada, we are also working to create a balance between policies stimulating innovation in the innovative pharma sector, versus generics getting more access to patents and reducing cost of health care.”*

50 The vaccines subsector comprises only 2% of the global pharmaceutical market.

51 For example, Prevnar for pneumococcus marketed by Wyeth and Merck's Gardasil for the human papilloma virus.

52 One industry interviewee explained: “Companies are very rational beings – they have limits on what they can research and thus must ration what they can allocate to vaccines. The markets that exist for HIV vaccines are the developing world, the companies aren't going to make the decision to invest in something that won't provide financial incentives. But we have to remember that vaccines are risky products - from a research perspective, they are scientifically very challenging. HIV and malaria have the same scientific hurdles. Vaccines in general cost more to research, take longer to develop, and the clinical trials are more expensive and more involved, you have to test on healthy people, there's a lot of risk from research through to launch to develop a vaccine. So overall, it's hard for them to justify beyond the PR benefit, beyond what they gain from being good corporate citizens. These firms are very interested in partnerships and looking for ways to do it together with public sector, but they shouldn't handle the burden of risk on their own.”

53 See Department of Finance Canada, News Release, 2007-011, “Canada's New Government Doubles Its Contribution to the Global Effort to Develop and Produce Vaccines for Diseases in Developing Countries” (9 February 2007), online: Department of Finance Canada <<http://www.fin.gc.ca/news07/07-011e.html>>. (On 9 February 2007, the Canadian Minister of Finance, The Honourable Jim

are attractive to industry players because a market is created and the financial risk is alleviated.

Interviewees from all sectors felt the private sector should be encouraged to think beyond “the bottom line” (i.e., financial profit) with respect to HIV vaccines R&D. Industry partners must see that investment in developing certain products has a benefit beyond material gain. Although some respondents were optimistic that corporate social responsibility is increasing, looking to examples in the tobacco and oil industry, the reality of business remains that investing in health solutions for the developing world is not attractive from a financial point-of-view.<sup>54</sup> Other informants felt that government may have to impose partnership agreements to ensure open access of IP, with respect to the use of public funds for HIV vaccines R&D, rather than relying solely on the good will of the private sector.

One interviewee summarized the most appropriate private sector roles as educating, advising and investing (both in-kind and financially) “to support moving principals forward and to be part of consortia, understanding that that also means giving something up, especially for some of these things like HIV or intellectual property related aspects or other types of health promotion and then commit further when there are actual achievements in terms of product development.” Other interviewees felt that the private sector is well-placed to advance an HIV vaccine program through opportunities to share both the risks and rewards

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Flaherty, announced US \$200 million for the Advance Market Commitment (AMC) to create a pneumococcal vaccine to benefit the world’s poorest nations:

The AMC is designed to create stronger incentives for industry to develop and produce vaccines that would meet the specific needs of developing countries. Participating donors will make a financial commitment towards the purchase cost of these vaccines. The AMC also aims to create an affordable market for vaccines in the long run, with a requirement that firms continue to supply developing countries with the vaccine after AMC funding concludes).

54 “But we’re seeing more and more that companies are looking for ways to create business models that can work, like GSK – Globalix – [a] product that will only sell in the developing world, despite there not being great markets. The big pharma are developing products and they have the sense that they are being criticized for not putting in the effort and resources. There’s risk even if they find an HIV vaccine that works, because then they face pressure to provide it for free or for very cheap. If they don’t, they’ll be demonized. In general, the public doesn’t understand business interests of companies.”



of R&D. Indeed the industrial sector may be more efficient in moving toward one vaccine concept as opposed to more scattered academic research. While there is expertise in vaccine research within academia, there needs to be a private sector recipient for the technology to come to fruition. The private sector could be stimulated through government assistance in creating R&D incubators, spaces, and facilities bringing together leaders in the biotechnology field.<sup>55</sup>

According to one interviewee, university researchers, and not industry (“big pharma”), are the source of innovation. The contribution of the pharmaceutical industry is in product quality control, large-scale production at lowest possible cost, and creation of distribution channels. Pharmaceutical companies have the infrastructure to conduct clinical trials and manufacture vaccines. IP can be a tool for managing partnerships between industry and academic researchers. Because industry will be very reluctant to fund something that is not protected by IP, industry partners can take the lead in developing patents for vaccine concepts and processes advanced by academic researchers. Industry stakeholders are generally very interested in PPPs and are eager to explore creative solutions that achieve mutually beneficial outcomes for all involved. However, it was recognized that many concepts in HIV vaccines research are at very early stages and not yet at the translational research stage where industry involvement becomes more productive.

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55 According to one interviewee, the most developed such facility in Canada is the MaRS Centre in Toronto, a convergence innovation centre and a not-for-profit corporation founded by leaders from the business and public sectors to improve commercial outcomes from Canada’s foundation of science and technology innovation. MaRS connects and fosters collaboration between the communities of science, business and capital through both co-location in the MaRS Centre and more broadly through catalytic programs, structured networks and the MaRS web portal. The MaRS Centre houses a large number of laboratory facilities for basic science and provides incubator space for new companies. These companies are assisted with legal issues, financing and management. There are business people, IP lawyers and venture capital in the same building as well as conference facilities and policy research. The purpose of the facility is capacity building and idea sharing. This model is one mechanism for helping Canadian companies and encouraging partnership with the Federal and Provincial governments. This model is also transferable to emerging economies and Canada could facilitate the development of similar organizations. See MaRS, “Home,” online: MaRS <<http://www.marsdd.com/MaRS-Home.html>>.

## Academia

All of the interviewees recognized that the academic sector is the main source of innovative ideas and approaches, and funding must be sustained to encourage such research.<sup>56</sup> The major challenge within the academic research culture is the “camped approach” to HIV vaccine development, and funding opportunities tend to favour one camp over another: “*Everyone thinks that their own compound is the best and going to save the world.*” Thus, funding needs to embrace many different approaches and foster openness to novel approaches. A more flexible funding structure, in turn, would help to create more openness with respect to collaboration and the sharing of IP.

Interviewees called on researchers to be more open to team-based approaches to HIV vaccines R&D. Researchers can have a very protective attitude towards their research projects, driven in part by the highly competitive and scarce funding environment. Many of the interviewees referred to the IAVI and the Gates Foundation funding as positive influences on IP sharing and collaboration.

Several interviewees referred to the culture differences with respect to IP between industry and academia. The focus for academic researchers is to advance and share knowledge. Academic researchers operate under a “publish or perish” system, and focus efforts on innovative research contributions. The need to publish is an IP issue and academic researchers may not be fully aware that they are at public fora (e.g., meetings, conferences) information which should be patented.<sup>57</sup> Academic researchers need to become savvier

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56 One of the interviewees noted Canada’s innovative approach to immunological research: “*The whole strategy in Canada has long been considered to be off the mainstream, using a strange accident of nature – the virus steals members of the host cell membrane molecules, HLA molecules, the virus has an imprint of the last person that was infected, and these HLA molecules could be targets for an immune response. We’d have to stimulate immune responses against foreign HLA. This was a completely different idea than immunizing against proteins of the virus.*”

57 “*If a researcher is working on something or makes a discovery that seems to be of real drug development interest, or patentable, then there needs to be someone at the university who already knows and can bring up to speed that person very quickly as to... ‘Don’t talk about this with colleagues, do not present this at meetings, do not show a poster of this, do not show a slide of this, until it’s patented. Don’t discuss it until it’s patented. Don’t discuss it with anyone.’ The trouble is, researchers don’t always know that, and they think, ‘Oh, it’s just a little meeting, or it’s just a seminar I gave at this university.’ But that’s*

with respect to IP,<sup>58</sup> as do university TTOs; at least one interviewee who had moved from academia to a spin-off biotechnology company expressed skepticism as to the competence of TTOs.<sup>59</sup> Several interviewees noted that TTOs at academic institutions (and even some individual researchers) need more education regarding IP protection and licensing strategies in the vaccine field. Indeed, TTOs may be a better target for education because only a small proportion of academic researchers will be inventing IP that is worthy of patent protection.

Finally, researchers who reported that they have attempted to conduct patent searches for compounds or processes relevant to their program of research have found that patent searching is a very difficult and time-consuming task; appropriate resources would have to be provided to research teams if the due diligence approach recommended by the Gates Foundation is to be implemented.<sup>60</sup>

## Potential Models for the Sharing of IP between Academic and Industry Researchers

Respondents were optimistic that it is possible both to stimulate vaccine R&D and maintain the integrity of the IP system. Models such as the GHAVE are based on the premise that success in HIV vaccines R&D will emerge only from inter-sectoral collaboration at a global scale – “people working alone in

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*public disclosure and then it makes it non-patentable. And really, academics are pretty naïve on that, by and large, unless they've been through the process before.”*

58 *“If academic researchers ever hope that their discovery will move into human testing and be developed by a drug company, they have to file a patent. They don't have to keep the IP, they can license it out, lock stock and barrel very quickly if they want, so that they don't have to be the one that maintains it and worries about it, but if they don't file it initially, then the discovery is not going to be of interest to anyone. Or someone will take their ideas and try to invent around it.”* [It should be noted that patents will not prevent, and, indeed, encourage “invent arounds.”]

59 *“Now in our case, even though we were at an academic institution, we had already hired our own lawyers, and we had filed even our very first patent search, so we didn't trust the university to do that for us because... sometimes when they are signing the initial patents, they're so full of holes that someone else could easily patent around you and it just renders the IP useless. You really need to know what you're doing upfront, you need to pay for the best legal help that you can get to do it, especially if it's a very important patent, like a platform patent.”*

60 See *supra* note 7 (for a discussion on due diligence).

*their labs, hoarding their ideas won't work*" – and that there needs to be effective strategies for technology transfer, commercialization and IP management. Here we discuss potential models that facilitate the sharing of knowledge and IP between academic and industry researchers.

### University Spin-off Companies

University spin-off companies are the model most often described by interviewees for transferring IP from academic to industry researchers. In this context, the academic institution, generally as assignee of the IP, grants an exclusive license to a spin-off company, which can then utilize it or sublicense it as specified by the terms of the license. The process is generally accomplished by TTOs; however, another innovative model has emerged through MaRS Centre in Toronto, which supports a company that works with universities and identifies potentially commercializable IP. In some cases, this company buys the IP or it shares the IP and then deals with commercializing and licensing to third parties.

There are several examples of spin-off corporations working on HIV vaccines. Variation Biotechnologies was started by three researchers in 2002 to advance research on HIV vaccines, focusing on a new platform technology that could be used for a range of vaccines against viruses that have a high level of antigenic variation (i.e., those viruses which frequently mutate). The founding scientists filed new patents on the technology, improving their existing patents and expanding their IP portfolio, and partnered with a business expert to lead the company's corporate development. Another interviewee described Coley Pharmaceutical Group as an example of a spin-off corporation.<sup>61</sup>

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61 Coley Pharmaceutical Group was formed on the basis of university-based research on a vaccine adjuvant, now branded VaxImmune™. The adjuvant has been made available to partners such as GlaxoSmithKline, Merck, and Novartis for evaluation in approximately 35 different vaccine clinical studies in the areas of oncology, infectious disease and biowarfare defense. With respect to HIV vaccines research, Immune Response Corporation performed primate studies using Coley's CpGs added to their vaccine candidate but due to financial difficulties, was not able to complete clinical trials. Coley's CpG adjuvant is also being used in research with HIV antigens by the National Institute of Allergy and Infectious Diseases (US) within the Vaccine Research Institute. Other companies have licensed CpGs for potential HIV vaccines and some of the candidate vaccines are in late pre-clinical stages.

### Public Private Partnerships

PPPs are another useful model widely pursued in the global vaccine and neglected diseases space.<sup>62</sup> While PPPs are likely to play an important role in accelerating HIV vaccines R&D, there is more to be learned about how best to structure them. PPPs have the advantage of increased access to research dollars but one commentator noted:

*What has happened with a number of colleagues is that they've found something interesting in their research. Then they find investors and the investors give them many millions of dollars to take their research further, which is great. But then their lab shifts from an academic focus to a commercial focus, which sacrifices the nature of the lab itself. The biggest struggle for researchers in PPPs is how to deal with the different environment when you now have investors with their commercial interests.*

### Other Sharing Models

Another suggestion was for TTOs to form associations and develop pools for technologies, "bundling" related technologies together into one portfolio to increase attractiveness to industry. A variation of this model has been used to commercialize the outputs from a publicly funded Canadian research network through Aggregate Therapeutics Inc. This company, formed by lead players in the Stem Cell Network, has an exclusive first right to negotiate the commercialization of stem cell technologies generated by the Network.<sup>63</sup>

Genome Canada is another model used in Canada to facilitate multi-stakeholder communication and collaboration. Genome Canada is a non-profit organization dedicated to funding, networking and information sharing for genomics and proteomics. Together with its six Genome Centres across Canada and with other partners, Genome Canada invests and manages large-scale research projects in key selected areas and new technol-

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62 See *supra* note 7.

63 Aggregate Therapeutics defines its role as follows: "The company uses a portfolio approach to commercialize therapeutic products for large markets with unmet clinical needs. It aggregates complementary technologies and leverages them across a common development infrastructure, management team and source of capital. This approach gives the company critical mass and lowers the risk, cost, and time to market in developing and commercializing therapeutic products." See Aggregate Therapeutics, "About us," online: Aggregate Therapeutics <<http://aggreatex.com/>>.

ogy development. Genome Canada also supports research projects aimed at studying and analyzing the ethical, environmental, economic, legal and social issues related to genomics research. The Genome Canada Board of Directors is composed of 15 members from industry and the scientific community in Canada. To date, Genome Canada has funded 114 large-scale research projects and science and technology platforms with a total investment to date of over \$1.4 billion with partner funding. Genome Canada's co-funding model includes 50% investment from the Federal Government and 50% from other sources.

Genome Canada recently launched a Technology Development Competition, which may also be instructive for HIV vaccines funding. Applicants were required to demonstrate social and/or economic benefits for Canada, and to include a plan for the transfer, dissemination, use or commercialization (as appropriate) of any inventions derived from the proposed technology development project.<sup>64</sup>

One of the biotechnology companies noted that they would like to explore creative partnerships with not-for-profit organizations, share profits with contributing organizations, and provide the vaccine at marginal or reduced cost in developing nations, such as through differential pricing arrangements with respect to IP. Several of the interviewees noted the need

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64 See Genome Canada, *Guidelines and Evaluation Criteria for Technology Development (Applied to Genomics and Proteomics Research) Competition* (Ottawa: Genome Canada, 2006) at 5, online: Genome Canada < <http://www.genomecanada.ca/en/portfolio/research/technology.aspx> >. Grant guidelines specify:

A clear commercialization process, which includes IP management and ownership, technology transfer and benefit sharing, must be defined and included in the full application. In anticipation of a successful outcome, the Genome Centre, potential host organization(s) and co-funding partner(s) should outline general terms that deal with the sharing of future benefits (e.g., equity, royalties, and repayment options, etc.) commensurate with the contributions of the respective parties. The plan must also describe how any new technology developed will be made accessible to any or all of Genome Canada-funded Science and Technology Platforms through a no-cost non-exclusive license. The plan should demonstrate how any technology developed would contribute to job creation and economic growth in Canada and their impact on society, quality of life, health, and the environment, as well as the creation of new policies in these areas. The commercialization process and technology access plan will be assessed during the due diligence/peer review process.

in general for more partnership opportunities between the private and academic sectors:

*It's about making sure there is an entry point for discussion so that if not all, at least some options are on the table and there is acknowledgement that the private sector can think about creative solutions and that it is not just business as usual. For the academic sector, it's the same concerns. Sometimes academics have blinkered understanding on how the world works so they need openness to experimenting and trusting partners, including private partners.*

Because there are already many global institutions focusing on HIV, some informants felt that Canada should focus its contributions nationally, such as by supporting a consortium of public and private researchers that builds upon specialized skills in Canada and coordinates research efforts to reduce wastage and duplication. One mechanism for sharing IP in a multi-sectoral research consortium would be under a confidentiality agreement with an understanding that its IP rights would be protected. Such an agreement would likely only function within smaller clusters of IP and well-defined parameters of what would be covered under the agreement. This model could work, for example, to test three different components of what might ultimately be a successful vaccine. Building such collaboration in a defined way would allow the benefits to flow to each party for their respective IP and would be attractive to all parties. On the other hand, resistance may arise if the collaboration was very fluid and too open, causing the parties to fear the risks of losing their IP contribution.

Other interviewees cautioned, however, that only global models for fostering research collaborations will be successful:

*I don't see science as being country-specific, I see it as very much an international effort. So, the main thing that Canada can do if they wanted to do something, would be to help Canadians become part of that global endeavor, and that may be funding for international collaborations, international meetings. But to do something just within Canada is not going to work – we're way too small, we have way too few people working on this compared to the worldwide scope and it's just not a country-specific effort. Canada should foster the global effort, helping Canada participate in those international endeavors.*

### Problems in Sharing IP between Academic and Industry Researchers

From the perspective of the industry partners, one of the main challenges of moving IP from academic research settings to the private sector is the

unrealistic expectations of TTOs. One interviewee, in particular, noted that some universities are unrealistic about the value that they've invested into IP relating to initial discovery phases of pre-clinical research.<sup>65</sup> Initial expectations from universities are unrealistic in both the royalties and license fees that they expect to receive from commercialization. Additionally, interviewees noted there are often long delays in negotiating MTAs with academic researchers because lawyers at the academic institutions' TTOs are "too aggressive." Interviewees also reported that some product developers are unwilling to collaborate and allow access to their materials.

This point was echoed by another interviewee who complained about the unrealistic expectations of TTOs regarding the value of the IP being generated in the public sector. He felt that TTOs don't always realize the complexity and the multiple elements that have to come together to have an effective HIV vaccine. Another frustration for private sector researchers is the difficulty of achieving cooperation amongst multiple TTOs in order to put together a comprehensive research program.

A further challenge is the variable quality of information being transferred to the private company once an IP agreement is signed with academia, NGOs or even biotechnology companies:

*Have they done everything to secure the IP? Do they have the records of sufficient quality? If there is clinical data involved, what is the quality control on the database so that one can use that data to employ in dossiers to support further clinical development etc. Are there any manufacturing pieces that have been done appropriately that the data is truly robust and data that you can trust?*

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65 "So they've filed a provisional patent, for example, and then when they're talking to companies about licensing it, the university tech transfer offices can be very naïve about what the value of that discovery is. Maybe there's a tiny bit of pre-clinical data on that to support the initial discovery, but that's really small compared to what drug development requires. But then they expect big huge up-front payments, big royalty payments, it's just not reasonable and they're not going to get those deals. They're overestimating the value of early stage discoveries because they're not savvy enough in that game to know that for that early stage, it's going to have limited value. And sometimes they have unrealistic expectations, and it's not to the university or inventor's advantage to try to push to get what they want. And they may end up just having companies just walk away, saying that it's so ridiculous that they're not going to work with them. So that's another issue between academia and companies."



This interviewee reported that one of the first steps in partnerships between academic institutions and private sectors is to educate public sector stakeholders on the industrial process, on IP, and even on proper note-keeping. Several of the interviewees noted that there is a great deal of variation between academic institutions with respect to IP licensing to private companies, and also a variation in their level of IP savvy. One of the interviewees from the private sector noted that Canadian universities are “easier to work with because they’re not quite as commercially savvy as some of the American universities, especially compared to big ones like MIT and Harvard. But they also, because of this naivety, may not have done a very good job of initially protecting their IP.”

Academic researchers felt forced into partnerships with industry investors because of the inadequacy of public (government-sponsored) funding resulting in a lack of capacity to protect their IP within these partnerships. These interviewees were also critical of institutional lawyers,<sup>66</sup> and bemoaned the reliance on TTOs to negotiate licensing agreements with companies and manufacturers. Researchers felt they knew little about the patenting process, despite having patented several compounds, because: “It all goes through the [university] research office – they deal with everything. I just sign the MTAs.”

TTOs need to be aware of the context surrounding specific IP and take it into consideration when drafting agreements for specific technologies: “So for example, HIV vaccine research would be quite different from software or some other type of licensing agreement. We need to make sure that TTOs looked to the difference between those.” In the HIV vaccine area, there is real concern that if university researchers do develop a vaccine product and the IP is handled by the TTO, the licensing of that product to industry must be constructed to avoid creating roadblocks to further research or vaccine availability. For example, one of the concerns encapsulated in OECD guidelines and emerging TTO practice is that TTOs retain rights for the research institution and license on a non-

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66 “The basic problem is that we just don’t get the government funding to really pursue creative ideas and follow them through. So how it ends up working is that you get the ideas out there and then the big pharma giants leap onto the IP for those ideas. If I really wanted to be a millionaire, I wouldn’t have gone into academia in the first place. In academia we get such poor advice about how to deal with patent and IP issues, most academic researchers steer away from it. They don’t want to get bogged down in legal issues, with a bunch of lawyers to make their lives miserable, and they just can’t afford the time that they need to put in to protect their ideas. As researchers, we just want to advance our ideas. And often institutional lawyers are totally overworked and leave us hanging on IP issues.”

exclusive basis. A humanitarian licensing strategy needs to be developed to allow universities to retain the discretion to license to developing countries for humanitarian use on differential terms such as cost.

On the positive side, one interviewee noted that IP negotiations between academic institutions and industry have become more streamlined as more universities now have TTOs or officers. In the past, university institutions were more reluctant to invest \$50-60,000 to help write patents because they were not sure what they would receive in return. According to one of the key HIV vaccine investigators, there can be mutually beneficial agreements between academic and industry partners with respect to sharing IP:

*Part of our agreement with the industry partner is sharing of the IP. What we own is the data that comes from the studies, and they already have patents on the compounds and the application of the compounds. The data belongs to us, and any publications which come out of the research. So, really IP has really not been an issue.*

## **Tools and Mechanisms for Canadian Contribution to Global HIV Vaccines Efforts**

All of the informants agreed that the development of an HIV vaccine is an important and far-reaching global public health priority. However, interview informants recognized the tension which exists between a global open science approach and the need to stimulate investment. Some of the respondents noted that there is no one comprehensive formal definition of what comprises a global open science approach, and thus the full impact of such an approach is unclear. Some of the interviewees described the global open science approach as “all about breaking down silos between different researchers who are currently working in isolation,” while others spoke of a range of levels of open access to scientific data, processes and products for all researchers in the field to pursue within their own research programs or, more ideally, within coordinated and collaborative research programs.

A discussion paper was commissioned by PHAC to clarify the key principle of global access within the context of the CHVI.<sup>67</sup> The work included

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67 San Patten, “Considerations Regarding Global Access in the Context of the Canadian HIV Vaccine Initiative” (Ottawa: Public Health Agency of Canada, 2008).

defining the operational components to fulfill the principle of global access within the CHVI, particularly in the production of clinical trial lots, and identifying global access considerations and implications that may influence design and delivery of the CHVI program components over the next five years. The principle of global access spans the entire product development pipeline: discovery, clinical trials, production, licensing, purchase, and delivery. While the ultimate focus for global access is the endpoint users of the vaccine, there are also considerations needed along the entire value chain, spanning from early pre-clinical studies all the way through to actual administration of the vaccine. Considerations for global access include: viral genetic diversity, population appropriateness, post-trial access, regulatory framework, equity (universality and accessibility), affordability, HIV vaccine distribution and knowledge sharing. Considerations of global access were also identified for discovery and social research and the manufacturing facility for pilot scale manufacturing of clinical trial lots. The consensus is that global access will best be achieved through a blending of enforcing regulations which promote knowledge sharing, affordability, participatory practice, and other elements of global access, as well as supporting the development of a social norm amongst the vaccine research community to promote these same principles.

The challenge of a global open science approach is that it may act as a disincentive for industry, deterring it from investing in HIV vaccines research. This is a well-recognized tension, and is one of the drivers for the public-private partnership model. Certain kinds of openness were described as more palatable than others.<sup>68</sup> An arrangement that would be attractive, for example, would be researchers sharing a set of immunogens and having the freedom to test these with different adjuvants or different delivery vehicles in a situation which would allow the sharing of IP to be quite easily defined. Researchers would be unlikely to share, however, “trade secret” information such as how to design the immunogens, the strategy employed, the platform technology, or how to improve the immunogens. Providing full access to this level of information would compromise the business interests of the partners holding the IP. However, while global open science is a laudable goal, it is difficult to define and even more difficult to operationalize:

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68 *“If you are talking about a purely open science approach, then that might eliminate the potential for the private sector to share and become a partner in endeavours now or in future. To the extent that IP rights could be maintained and protected, then open science is a great idea.”*

*The problem with open science in general is that we don't know enough about how it works and how novel strategies will pan out. But if any area is ripe for taking that risk, then it is this area of HIV. We should be bold and creative and this is one example where it should be tried – as a public health emergency, this is unparalleled. I think there is a reasonable prospect for improvement over what is being done right now.*

One interviewee was optimistic that facilitating an open science model for global access and encouraging innovation are not necessarily mutually exclusive:

*A lot of research shows that people want to be part of the solution not part of the problem. They would rather engage in a project with altruistic goals. You see the evidence around world – Wikipedia, PIPRA... altruism is a powerful motivator. But it is not the only motivator. There is a growing recognition that when people collaborate, the quality of research improves. So from a selfish perspective, open science and open methods can enhance individual and institutional performance.*

Most of the interviewees approved the approach to Global Access taken by the Bill & Melinda Gates Foundation's Grand Challenges in Global Health Initiative and Canada's continued contribution to international PPPs and other efforts.<sup>69</sup> We have discussed other international efforts at enhancing global access, such as patent clearinghouses and research material patent pooling in the companion paper, all discussed by the interviewees.<sup>70</sup> But the one model emphasized by the interviewees is the National Institutes of Health (NIH) AIDS Research Reference Reagent Program. The Program distributes free of charge 8,400 registered viruses, antibodies, proteins, peptides, cell lines, recombinant DNA clones, antivirals and expression vectors:<sup>71</sup> *"The way the program works is that investigators deposit their reagents and the NIH will pay for producing those reagents. So if we come up with some kind of antibody, we give it to them and they produce it for free. Any scientist in the world can access those reagents. I would say that program has really accelerated HIV vaccines."*

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69 See *supra* note 7.

70 *Ibid.*

71 NIH AIDS Research & Reference Reagent Program, "Home," online: NIH AIDS Research & Reference Reagent Program <<https://www.aidsreagent.org/Index.cfm>>.

One additional point to note about patent pooling is that a pool may be created through the use of either voluntary or compulsory licensing via the mechanism provided in the *Doha Declaration*.<sup>72</sup> One of the interviewees encouraged the HIV vaccines research sector to build a patent pool that will allow researchers to “*think laterally about patents,*” along with questions of research and manufacturing capacity and national R&D capacity, national IP law, and corporate law (e.g., product liability). While developing a patent pool is complex due to the need to align it with all the relevant laws of all of the nations involved, it could be much more effective than bilateral mechanisms currently available, such as simple compulsory licenses. Patent pooling, however, is currently not possible under Canada’s compulsory licensing regime, the Canadian Access to Medicines Regime (CAMR).<sup>73</sup> A patent pool could also allow developing countries access to: “*the technical know-how associated with the technology not just the bare bones but also the research, not just looking at patents but also at relationships that will evolve between those involved in the pool and then those commercial entities that want to manufacture the product.*”

Global access may be facilitated by building R&D and manufacturing capacity in developing countries. Interviewees cited examples which demonstrate that building the research capacity of developing countries in turn allows them to create their own IP (e.g., China, India, South Africa, Brazil, and Mexico). Many of these countries have high R&D capacity, or could develop such capacity through enhanced partnerships with organizations and institutes in the North or in the South. Interviewees noted that these partnerships should be structured so as to allow the IP to be developed and owned by the researchers in developing countries.

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72 See World Health Organization, “Doha Declaration on the TRIPS Agreement and Public Health,” online: WHO <[http://www.who.int/medicines/areas/policy/doha\\_declaration/en/index.html](http://www.who.int/medicines/areas/policy/doha_declaration/en/index.html)>. (In 2001, WTO Members adopted a special Ministerial Declaration at the WTO Ministerial Conference in Doha to clarify ambiguities between the need for governments to apply the principles of public health and the terms of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)).

73 For a review of the CAMR, see Richard Elliott, *Getting the Regime Right: Compulsory Licensing of Pharmaceuticals for Export: Brief to the House of Commons Standing Committee on Industry, Science and Technology regarding Canada’s Access to Medicines Regime* (Ottawa: Canadian HIV/AIDS Legal Network, 2007), online: Canadian HIV/AIDS Legal Network <<http://www.aidslaw.ca/publications/interfaces/downloadFile.php?ref=1058>>.

Ultimately, countries may be able to develop their own affordable vaccines, such as the Instituto Butantan in Brazil, which is developing its own HPV vaccine *de novo*. However, at the research level, researchers in the developing world can in-license technologies and pay for these. A biotechnology company in India called SHANTHA Biotech, for example, has developed a hepatitis-B vaccine using genetic engineering. SHANTHA licensed some technologies and innovated their own processes, decreasing the cost of the vaccine by up to 20 times by making the vaccine in-country and ultimately achieving much greater access. UNICEF now purchases 40% of its hepatitis-B vaccine from SHANTHA.

Finally, global access may be enhanced through market-based financing mechanisms to accelerate the development and availability of HIV vaccines. One such model is the Advance Market Commitment (AMC), which guarantees that funds will be available to purchase vaccines once they are developed and produced, thereby eliminating the risk that a country will not be able to afford to introduce a high-priority vaccine into its national program.<sup>74</sup> The AMC establishes a market that the biotechnology and pharmaceutical industries currently perceive to be too small and too unpredictable.

Several interviewees felt that AMCs are a promising model to encourage research into, and eventual access to, HIV vaccines, but they also noted both positive and negative aspects of AMCs. Interviewees recognized that with low private sector interest in HIV vaccines R&D, AMCs may be a promis-

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74 An AMC for vaccines is a financial commitment to subsidize the future purchase (up to a pre-agreed price) for a vaccine not yet available if an appropriate vaccine is developed and if it is demanded by developing countries. Bound by legal agreements, sponsor countries or foundations agree to provide financial commitments to subsidize the purchase cost of future vaccines for a period of time, and vaccine manufacturers agree to meet criteria for vaccine effectiveness and to provide the vaccine at affordable prices. An AMC is not a purchase guarantee, as industry will only receive the subsidized price if the product meets targeted standards and countries demand the product. AMCs complement existing prevention, treatment, and research efforts by providing a financial commitment to subsidize the future purchase of a vaccine not yet available. The commitment itself has no cost unless and until an appropriate vaccine is developed. This means that an AMC does not divert money from being invested in existing solutions to disease control while the new vaccines are being developed. See Advance Market Commitments for Vaccines, "Home," online: Vaccine AMCs <<http://www.vaccineamc.org/index.html>>.

ing way for government to create fiscal incentives and market competition. AMCs are an attractive model for vaccines because the model accommodates multiple stakeholders' interests; government can create market interest for HIV vaccines by investing resources within standard market dynamics. AMCs recognize how markets work, the shortfalls of market demands with respect to producing public health goods such as HIV vaccines, and intervene through a market solution, rather than developing new systems for getting products developed and distributed: *"The AMC project is all about risk reduction, taking away the question from the company that they'll be guaranteed some kind of return on investment, or at least break even."*

One interviewee noted that AMCs are more agreeable to the general public as well, because developed country governments are not burdened solely with ensuring HIV vaccines R&D or global access to HIV vaccines.

Within the Government of Canada, the Department of Finance has been leading Canada's participation in the development of AMCs, in particular, determining the financing role that Canada will play, developing Canada's position on AMCs, determining relationships with other donors, and overseeing interdepartmental relations. Other departments – including CIDA, Health Canada, PHAC, DFAIT and Industry Canada – are collaborating with the Department of Finance to work through issues such as disease choice, evaluation issues and intellectual property. In February 2007, Canada, Italy, Norway, Russia, the United Kingdom, and the Bill & Melinda Gates Foundation committed US\$1.5 billion to launch the first AMC to help speed the development and availability of a new pneumococcal vaccine which is expected to save the lives of 5.4 million children by 2030. This pilot is in the process of being designed to demonstrate both the feasibility of the AMC mechanism and its impact on accelerating vaccine development, production scale-up, and introduction. Once established, the pneumococcal AMC will support industry and government efforts to prevent unnecessary pneumococcal deaths in developing countries. Importantly, it will also enable stakeholders to assess quickly the impact of the AMC mechanism to determine if AMCs will be able to accelerate other health priorities such as vaccines against malaria. According to an interviewee leading Canada's role in the AMC, the hope is to have the pneumococcal vaccine AMC fully operational by December 2007.<sup>75</sup>

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75 Presently, the six donors are working on details of how each donor will make a commitment, how to fully operationalize the AMC, how to raise awareness

There will be an independent assessment commitment to ensure that pneumococcal vaccines meet eligibility criteria. Vaccines will be purchased only if they meet pre-determined standards of efficacy and safety, and if developing countries ask for them. Intellectual property for the eligible vaccine would rest with the company. One of the interviewees noted that while the AMC donors set the minimum bar for the vaccine standards, due to competition forces, industry may strive to exceed the standard, thereby allowing developing countries a choice as to which product they purchase.

The next likely candidate vaccines to be considered for an AMC are for malaria and possibly tuberculosis.<sup>76</sup> According to one of the interviewees, there are many reasons why HIV was not chosen by the Expert Committee as the first test case for the AMC pilot:

The science around an HIV vaccine is not at all clear. We don't even have scientific consensus that a vaccine is possible and even if it is possible, the timelines are so long before an HIV vaccine would be available for the market. Therefore, if we used HIV as a test case for AMCs, we wouldn't be able to demonstrate results until very far into the future. Also, it's very difficult to set out the criteria for an HIV vaccine and thus very difficult to detail the AMC eligibility criteria for HIV vaccine research. Whereas pneumococcal already has vaccines in the pipeline, and we can influence the direction of the pipeline, and see if industry is responsive to the AMC. We really hope to use AMC as a mechanism to change R&D for developing

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amongst industry, and putting together finance structures which are credible to industry. An important question for AMCs is the appropriate amount of financing that would help repay the R&D specific to getting products tailored to developing countries. In terms of competition, the size of the AMC becomes very important; a smaller AMC amount may only provide market opportunity to one company. Demand forecasting is another key issue for AMCs, as they are only paid out once there is demand from developing countries and only once the vaccines are delivered by a company to developing countries.

76 The Expert Committee recommended that a second demonstration AMC for a malaria vaccine be explored to stimulate early R&D investment and to pilot the impact of the AMC on early stage vaccines. The Expert Committee recognized there was a strong case for both malaria and tuberculosis AMCs. After careful consideration, the Committee recommended malaria for the pilot because the vaccines are at more advanced stages and are more likely to yield a timely and measurable response to the AMC.



country issues in which industry doesn't otherwise have an interest, so there's applicability well beyond vaccines.

## Conclusion

Canada is well placed to contribute to the global initiatives to develop a safe, effective and accessible HIV vaccine. The roadblocks are primarily technical, given the difficulties in developing such a vaccine,<sup>77</sup> and related to funding. Interviewees felt that inadequate funding, and not IP, was the greatest roadblock to HIV vaccine research in Canada. Researchers in particular recommended several different funding models that might be considered, from operating grants to collaborative research grants, and should be consulted further on any proposed funding models developed by CHVI.

Commercialization activities, including patenting, and large public support for research with concomitant requirements for access in the context of HIV vaccine research may not be contradictory. Indeed, the holding of patents by public sector researchers or institutions or public private research consortia may be required to guarantee both private investment and global access. Patents give the patent holder the right to control the use, manufacture, sale, etc., of patented products, generally through licensing agreements. In this context, the most effective strategy may be "defensive" patenting to ensure that vaccine-related inventions are licensed according to a global access strategy and Canadian government policies.

There are already policies from public funding agencies such as NIH and CIHR designed to encourage access to research outputs. CIHR and NIH current policies on publications and data are the first step towards recognizing the need for policy intervention in this arena. However, for products and processes arising from HIV vaccine research, further guidelines should be developed to ensure that licensing models follow a Global Access Strategy. Some examples of guidelines to this effect are the OECD Guidelines for the Licensing of Genetic Inventions and the Gates Global Access Program. Such licensing guidelines include non-exclusive licensing, retention of research institution rights to conduct research, march-in rights, and humanitarian provisions such as differential royalty/pricing structures for developing/developed countries.

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<sup>77</sup> See *supra* note 7.

A key finding from our interviews was that public sector researchers may not have the knowledge required to adequately protect IP. In addition, some institutional TTOs tend to be over-zealous and unrealistic in the percent royalties that they expect to receive from commercialization, asking for unreasonable license fees, and creating long delays in negotiating MTAs. HIV vaccine researchers should be offered training on how to protect and license IP in the context of a Global Access Strategy for HIV vaccine R&D. In addition, institutional TTOs and Research Offices may benefit from training on how to protect and license IP and negotiate collaborative research agreements in the context of a Global Access Strategy for HIV vaccine R&D.

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## **APPENDIX 1**

### **Canadian Patent Landscape of HIV Vaccine-Related Technologies**

### **INTERVIEW GUIDES**

#### **Interview Questions for Researchers**

1. Please provide us with an overview of your background and current involvement in HIV vaccines research and development.
2. a) What is the general nature of your research?  
b) Please describe the main research questions that you are addressing with respect to HIV vaccines.
3. What would you identify as the main non-science challenges in your HIV vaccines research?
4. Have you ever conducted a search for patents relevant to your research field or are you aware of any such patents? (Please give details).
5. Have you encountered any roadblocks in your research due to negotiating licenses for patented elements/processes needed to pursue a line of vaccine research? If so, please describe these patent-related roadblocks.
6. Have you ever requested research materials and had that request denied? If so, please describe what happened.
7. Have you ever had any significant delays in your research due to transfer of material and the negotiation of material transfer agreements? If so, please describe what happened.
8. How do you respond to material transfer requests?
9. Please tell us about the patenting and licensing strategies within your commercialization plan for HIV vaccines-related compounds or technologies.
10. What challenges have you experienced, or would you anticipate, in the transfer of intellectual property from academic or non-profit researchers to product developers/manufacturers?

11. Do you feel that there needs to be greater sharing of intellectual property between scientists, both within and between private/public sectors? [in the sphere of HIV vaccines only]
12. Are you supportive of a global open science approach for HIV vaccines? What actions or models would you like to see implemented in Canada to facilitate a global open science approach and to remove restrictions on freedom of operation?
13. How would these actions to encourage an open science approach be balanced against the need to stimulate innovation?
14. Overall, what recommendations would you give to the Government of Canada to encourage acceleration of HIV vaccines research? What activities could/should be undertaken by the private and academic sectors?
15. Do you collaborate with HIV vaccine researchers internationally? If so, which countries and what is the extent of this collaboration?
16. Could you provide us with 10 keywords for conducting a patent search in your field?

## **Interview Questions for Policy Makers**

1. Please provide us with an overview of your background and current involvement in HIV vaccines research and development. (probes: position, department, sector, programs, funding bodies)
2. What would you identify as the main non-science challenges the field of HIV vaccines research?
3. When working with your constituency (researchers, industry, manufacturers), have you encountered any patent-related roadblocks related to licenses for patented elements/processes needed to pursue a line of vaccine research (e.g., proteins, biomarkers, assays, immune monitoring technologies/processes, manufacturing technologies/processes)? If so, please describe these patent-related roadblocks.

4. What challenges would you anticipate in the transfer of intellectual property from academic or non-profit researchers to product developers/manufacturers?
5. What do you feel is an appropriate role for government stakeholders in addressing the non-science barriers to HIV vaccines research? What is an appropriate role for the private sector? For the academic sector?
6. Do you feel that there needs to be greater sharing of intellectual property between scientists, both within and between private/public sectors?
7. Would you be supportive of a global open science approach for HIV vaccines?
8. How would these actions to encourage an open science approach be balanced against the need to stimulate innovation?
9. What actions or models would you like to see implemented in Canada to facilitate a global open science approach and to remove restrictions on freedom of operation? (prompt on licensing provisions such as humanitarian licensing, creative commons type licensing, viral licensing terms in favour of scientific commons)
10. Overall, what can, or should, the Government of Canada do to encourage acceleration of HIV vaccines research?

## **Interview Questions for Policy Experts**

1. Please provide us with an overview of your background and current involvement in HIV vaccines research and development.
2. What would you identify as the main non-science challenges in the field of HIV vaccines research?
3. When working with your constituency (researchers, industry, manufacturers), have you encountered any patent-related roadblocks related to licenses for patented elements/processes needed to pursue a line of vaccine research (e.g., proteins, biomarkers, assays, immune monitoring technologies/processes, manufacturing

technologies/processes)? If so, please describe these patent-related roadblocks.

4. What challenges would you anticipate in the transfer of intellectual property from academic or non-profit researchers to product developers/manufacturers?
5. What do you feel is an appropriate role for government stakeholders in addressing the non-science barriers to HIV vaccines research? What is an appropriate role for the private sector? For the academic sector?
6. Do you feel that there needs to be greater sharing of intellectual property between scientists, both within and between private/public sectors?
7. Would you be supportive of a global open science approach for HIV vaccines?
8. How would these actions to encourage an open science approach be balanced against the need to stimulate innovation?
9. What actions or models would you like to see implemented in Canada to facilitate a global open science approach and to remove restrictions on freedom of operation?
10. Overall, what can, or should, the Government of Canada do to encourage acceleration of HIV vaccines research?