Current State of HIV Vaccine Research

This info sheet reviews the state of HIV vaccine research globally and in Canada as of March 2002.

This is one of a series of 8 info sheets on HIV Vaccines in Canada.

CANADIAN HIV•AIDS LEGAL NETWORK | RÉSEAU JURIDIQUE CANADIEN VIH•SIDA

Canadian Strategy on HIV/AIDS

The Global Effort

Some progress has been made in the global effort to find an HIV vaccine. Advances in molecular biology and basic HIV research have led to the development of promising strategies. Some experimental vaccines have shown the ability to protect non-human primates from infection by a virus closely related to HIV. A number of candidate vaccines have been shown to be safe in small-scale (Phase I and II) clinical trials and to trigger HIV-specific immune responses.

Some people repeatedly exposed to HIV resist infection and mount HIV specific immune responses, which provides important clues for the design of an effective HIV vaccine. There is a growing scientific consensus that an effective HIV vaccine is possible.

Since 1987, when the first HIV vaccine trial was conducted, about 30 candidate vaccines have been tested in approximately 60 phase I/II clinical trials, involving more than 10,000 healthy human volunteers. Two candidate vaccines are undergoing large-scale (Phase III) efficacy evaluation in North America, the Netherlands, and Thailand. The final results from these trials are expected in 2003. A Phase III trial of another candidate vaccine is scheduled to start in early 2003 in Thailand, with results expected by 2007.

No precise figures are available on the amount of money being spent on HIV vaccine research globally, but estimates range from $US 450 to 600 million a year. This represents less than one percent of the spending on all global health research and development.

HIV Vaccine Research in Canada

In Canada, some work is being done to develop candidate HIV vaccines in the laboratory and to test these vaccines on animals. There have been no Phase I/II clinical trials of candidate HIV vaccines in Canada. There is one Phase III HIV vaccine trial currently operating in Canada – a multinational trial of the AIDSVAX® B/B Gp 120 experimental vaccine produced by VaxGen Inc.

Aside from the AIDSVAX trial, about $CAN 2.14 million is being spent each year in Canada for HIV vaccine research. The Canadian Network for Vaccines and Immunotherapeutics (CANVAC) has been investing about $CAN 1.3 million annually in HIV vaccine biomedical research and $CAN 140,000 annually in HIV vaccine behavioural research. The Canadian Institutes of Health Research (CIHR) has been investing about $CAN 700,000 annually in HIV vaccine research.

In addition, the Canadian International Development Agency provided a two-year grant of $CAN 5 million in 2001 and 2002 to the International AIDS Vaccine Initiative to support international HIV vaccine development.

The AIDSVAX Trials

AIDSVAX B/B is a candidate vaccine designed to prevent HIV infection. It was developed by VaxGen, a California biotechnology company. This vaccine is designed to work against the B subtype of HIV, found primarily in North America, Western Europe, Australia, the Caribbean, and South America. AIDSVAX B/B is being evaluated in a Phase III clinical trial underway in Canada, the United States, and the Netherlands. VaxGen has also developed a similar vaccine, AIDSVAX B/E, which is designed to prevent infection with HIV subtypes B and E, primarily E (the subtype found extensively in Asia). A Phase III clinical trial involving AIDSVAX B/E is underway in Thailand.

The North America/Netherlands trial started in 1999 and is scheduled to be completed at the end of 2002. The trial has enrolled over 5400 participants, of whom 291 are in Canada. There are three Canadian trial sites: Vancouver, Toronto, and Montréal. The primary objectives of the trial are:

- to determine if the vaccine helps prevent HIV infection in people who are at risk for getting HIV through sexual activity; and

- to determine if the vaccine is safe compared with the placebo when given to large numbers of people who are at risk for HIV infection.

In addition, the trial is trying to determine if the vaccine also helps slow the rate of disease progression in people infected with HIV, and if people change their sexual activity or other risk behaviours while they are in the study. Results from the North America/Netherlands trial are expected in early 2003.

Recruitment for the AIDSVAX Trials

At the three Canadian sites, participants had to fulfil the following entry criteria: men who have sex with men; 18-60 years old; HIV-negative; at risk of HIV infection; not an injection drug user; available to participate in the study for three years.

"At risk of HIV infection" was defined as having engaged in anal intercourse with someone other than a regular HIV-negative partner in the 12 months preceding enrolment.

The US sites had similar entry criteria but also recruited some HIV-negative women who had HIV-positive sexual partners or who were considered to be at higher risk of HIV infection. The trial in Thailand recruited HIV-negative injection drug users with a high risk for bloodborne transmission of HIV.

At the three Canadian sites, the following approaches were used to recruit participants: direct referrals from physicians; direct referrals from workers at AIDS service organizations; distribution of brochures and posters in STD clinics and gay venues; community forums; advertisements in the gay press; publicity through media articles; and word of mouth.

In Vancouver and Montréal, existing cohort studies involving gay and bisexual men were also a source of recruitment. In Montréal, some people enrolled simultaneously in the cohort study and the AIDSVAX trial.

The information in this series of info sheets is taken from *HIV Vaccines in Canada: Legal and Ethical Issues: An Overview*, prepared by the Canadian HIV/AIDS Legal Network. Copies of the paper and info sheets are available on the Network website at www.aidslaw.ca/Maincontent/issues/vaccines.htm and through the Canadian HIV/AIDS Clearinghouse (www.clearinghouse.cpha.ca). Reproduction is encouraged, but copies may not be sold, and the Canadian HIV/AIDS Legal Network must be cited as the source of this information. For further information, contact the Network at info@aidslaw.ca. **Ce feuillet d'information est également disponible en français.**

Funded by Health Canada, under the Canadian Strategy on HIV/AIDS. The views expressed are those of the author and do not necessarily reflect the views or policies of the Minister of Health.

Why We Need a Canadian HIV Vaccine Plan

This info sheet explains why Canada must increase its investment in HIV vaccine development and delivery, and concludes that Canada needs a formal HIV vaccine plan.

This is one of a series of 8 info sheets on HIV Vaccines in Canada.

CANADIAN HIV·AIDS LEGAL NETWORK | RÉSEAU JURIDIQUE CANADIEN VIH·SIDA

Canadian Strategy on HIV/AIDS

The Need to Act at Home

Canada needs an HIV vaccine for the following reasons:

- **HIV/AIDS poses a threat to the health of Canadians**. As of the end of 1999, it was estimated that there were almost 49,000 people living with HIV/AIDS in Canada. The epidemic in Canada is growing among women, Aboriginal people, and men who have sex with men, and remains a serious problem among injection drug users, prisoners, street youth, and immigrant communities from endemic countries.
- **Existing treatments have limitations**. The antiretroviral treatments available today are unable to cure the disease or eliminate the virus entirely. Treatment is costly and lifelong, and the treatment regimens are difficult to follow. The treatments can produce adverse effects, some of which can be severe. As well, the treatments can fail due to the emergence of drug-resistant strains of HIV.
- **Existing prevention methods have had limited success**. Behaviour is influenced by many factors – environmental, political, social, religious, cultural, economic, educational, and psychosocial – so getting people to use condoms and sterile injection equipment regularly is a formidable challenge. It is often difficult for people to maintain safer sexual behaviour over a lifetime.

The rise in infection rates among specific populations is evidence of the fact that current prevention and treatment strategies have not been successful in stemming the tide of the epidemic. In addition to strengthening our current efforts (including by addressing the underlying causes of disease, such as poverty, marginalization, discrimination, etc), new strategies such as vaccine research and development must be urgently explored.

Up to now, work on HIV vaccines in Canada has been fairly limited. No funds have been specifically earmarked for HIV vaccine research. No Phase I/II human trials of HIV vaccines have taken place in Canada. No work has been done to plan for the delivery of an eventual HIV vaccine. Canada can and should do more.

The Need to Act Globally

Conducting more research on HIV vaccines in Canada would benefit not only Canadians, but also people from other countries. HIV/AIDS is the world's most deadly infectious disease. As of December 2001, over 40 million people were living with HIV/AIDS. Already, 25 million people have died of AIDS-related causes. An estimated five million people were newly infected with HIV in 2001 –

more than 13,500 every day. More than 13 million children worldwide have been orphaned by HIV/AIDS. In 16 African countries, between 10 and 20 percent of the adult population has HIV.

AIDS is overwhelming health-care systems and national economies. The UN estimates that the medical and human costs of AIDS have already reversed social and economic development in 20 countries. In sub-Saharan Africa, household incomes have fallen by half and business profits have decreased by 20 percent due to AIDS deaths. By 2010, South Africa's gross national product will be more than 17 percent smaller than it would have been without AIDS.

Furthermore, increasing access to antiretroviral drugs and other treatments in the developing world continues to be difficult, due to cost and limited health infrastructures. Most people in the developing world cannot afford antiretroviral drugs or even most of the treatments for opportunistic infections. A preventive vaccine will be more affordable than current treatments.

We need to act now to ensure that the delays experienced in delivering HIV treatments to the world's poor are not repeated when an effective AIDS vaccine becomes available. Developing plans now is critical not only to ensure vaccine development, but ultimately to deliver a vaccine expeditiously.

Canada is party to a number of human rights treaties imposing obligations that arguably require us to do more. And as one of the richest nations in the world, Canada also has a moral obligation to contribute generously to the international effort to develop HIV vaccines.

Conclusion

The case for investing in HIV vaccine development and delivery is clear. Our experience with other infectious diseases is encouraging. Smallpox was eradicated in 1977 because of an effective vaccine. Polio has been eliminated in the Americas due to an effective vaccine, and projections are that it will be eliminated globally by the end of 2005. Measles and yellow fever have been controlled by vaccines. Yet only two candidate HIV vaccines have reached large-scale efficacy trials, the final stage of testing in humans. The pace of research needs to be accelerated.

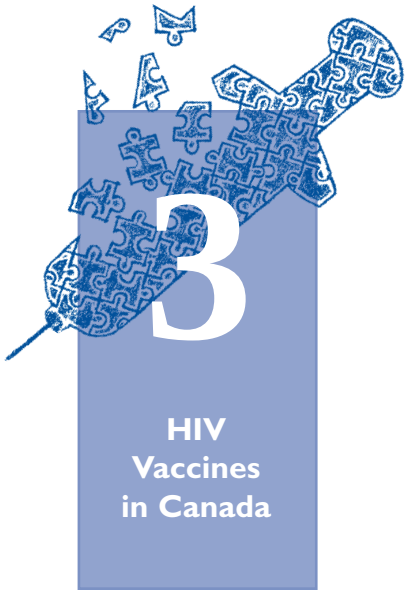
Canada should commit significant additional resources to HIV vaccine research, both in Canada and in developing countries, and should develop an agenda for HIV vaccine development and delivery. This would best be accomplished through the creation of a formal Canadian HIV Vaccine Plan.

Recommendations

1. Governments, the pharmaceutical industry, researchers, and HIV/AIDS community organizations should make a firm commitment to an accelerated and sustained program of HIV vaccine research in Canada.
2. Federal and provincial governments and the pharmaceutical industry should substantially increase their investment in HIV vaccine research in Canada.
3. Health Canada should coordinate, and provide funding for, the development of a Canadian HIV Vaccine Plan. The Plan should be prepared in consultation with the provinces and territories, HIV/AIDS community organizations, HIV researchers, private industry, health-care providers, public health, and other stakeholders, and should be developed by 1 October 2003. It should contain a development component and a delivery component. The development component should focus on those areas where Canada has experience and expertise and can therefore have the greatest impact.
4. Health Canada, through the Canadian HIV Vaccine Plan, and with the participation of HIV/AIDS community organizations, should mobilize public opinion and support for HIV vaccine development and delivery.
5. The federal government should significantly increase funding for international HIV vaccine efforts. It should participate actively in attempts to ensure global coordination of HIV vaccine development.

The information in this series of info sheets is taken from *HIV Vaccines in Canada: Legal and Ethical Issues: An Overview*, prepared by the Canadian HIV/AIDS Legal Network. Copies of the paper and info sheets are available on the Network website at www.aidslaw.ca/Maincontent/issues/vaccines.htm and through the Canadian HIV/AIDS Clearinghouse (www.clearinghouse.cpha.ca). Reproduction is encouraged, but copies may not be sold, and the Canadian HIV/AIDS Legal Network must be cited as the source of this information. For further information, contact the Network at info@aidslaw.ca. **Ce feuillet d'information est également disponible en français.**

Funded by Health Canada, under the Canadian Strategy on HIV/AIDS. The views expressed are those of the author and do not necessarily reflect the views or policies of the Minister of Health.



Involving Communities in the Conduct of Clinical Trials

This info sheet discusses why communities, including people with HIV/AIDS, should be involved in the design and implementation of HIV vaccine trials. It also describes how communities can become involved.

This is one of a series of 8 info sheets on HIV Vaccines in Canada.

CANADIAN HIV·AIDS LEGAL NETWORK | RÉSEAU JURIDIQUE CANADIEN VIH·SIDA

Canadian Strategy on HIV/AIDS

Why Community Involvement Is Important

Governments, pharmaceutical manufacturers, researchers, and communities need to work together on HIV vaccine development. Communities should be involved in the design and implementation of vaccine trials because they can make a meaningful contribution to the success of the trials. They can help to ensure:

- that the trials meet appropriate scientific and ethical standards, including adequate informed consent, education on safer sex and needle use, and protection from harm;
- that the trials are relevant to the targeted populations; and
- that the trials are accepted by these populations.

Communities can help to improve the design of the trials, which in turn can lead to better recruitment and retention of volunteers. The involvement of the community will also generate grassroots support for the development and eventual delivery of an HIV vaccine. This support is critical to obtaining scientific, political, and economic support at higher levels.

Another reason for involving the communities that will be targeted by a vaccine trial is that the trial may generate undue optimism, and this may make it necessary to modify and strengthen prevention messages. The presence of an HIV vaccine trial in a community, and the potential this offers for the discovery of a successful vaccine, might create a false sense of security on the part of the trial participants and the community at large. This false sense of security could lead people to think that they are no longer at risk for HIV infection or that the risk has been significantly reduced. This might lead to increased risk taking by some individuals. Communities that are targeted by vaccine trials therefore have an important role to play in ensuring that appropriate prevention messages are delivered.

How Communities Can Participate

Community representatives can contribute to the design and implementation of an HIV vaccine trial by:

- participating on research ethics boards that review trial protocols;
- educating people in the community about the proposed trial;
- relaying the concerns of the community to trial organizers;
- providing input to trial organizers on the design of the trial;
- supporting recruitment to the trial;
- monitoring the trial as it is being implemented;
- working to minimize the possibility that undue optimism about the efficacy of a vaccine could lead to increased risk behaviour among trial participants or in the community generally;
- helping to disseminate the trial results; and

- advocating for effective delivery when a vaccine becomes available.

Community organizations will need to be supported in their efforts to fulfil these roles.

The Role of Community Advisory Boards

One way to structure community involvement in HIV vaccine trials is through the use of community advisory boards (CABs), which are usually made up of volunteers from the target community. CABs can help in several ways:

- **CABs can help researchers better understand the target communities**. They can provide researchers with advice on: how to recruit and retain research subjects; how to provide prevention counselling to trial participants; how to undertake community relations; and how best to disseminate information about the trial in the community. CABs can educate researchers on the cultural sensitivities of the target communities.
- **CABs can assume a leadership role in the design of some aspects of the trial**. They can provide valuable input on: (a) measures to minimize risk to trial participants; (b) disclosure of information about the trial to participants; and (c) the informed-consent process. CABs can also review the written materials produced by researchers for use before and during the trial.
- **CABs can fulfil an education role within the community**. They can educate the community about vaccine research issues in general and about the specific vaccine trial they are involved with. They can also provide a forum for trial participants to raise issues or concerns.

Thus, CABs can provide a useful forum for communities, NGOs, and researchers to share information, problem solve, and work to improve the trial. In the case of the AIDSVAX trial, CABs were established in each of the three Canadian sites: Vancouver, Toronto, and Montréal.

The Need to Involve People Living with HIV/AIDS

People living with HIV/AIDS should participate in the design and implementation of preventive vaccine trials for the following reasons:

- They are an integral part of the community and play a role in HIV prevention.
- Research on preventive vaccines may yield information that can be used to develop therapeutic vaccines, particularly with regard to how the preventive vaccines stimulate the immune system. People living with HIV/AIDS will be interested in obtaining and disseminating the scientific information generated by the preventive vaccine trials.
- The involvement of people living with HIV/AIDS will enable the community to speak with one voice in advocating for more vaccine research and for the simultaneous study of new agents as both preventive and therapeutic vaccines (wherever possible).
- They need to hear the message that testing an experimental vaccine does not mean that a cure is on the horizon.
- Having HIV-positive people involved at the outset can help ensure that the allocation of resources to vaccine research does not detract from the provision of care, treatment, and support to people living with HIV/AIDS. This may help avoid schisms between HIV-positive and HIV-negative people in the community.

Recommendations

1. Trial organizers and governments should provide funding for community organizations to educate communities about HIV vaccine research and to participate in the design and implementation of HIV vaccine trials.
2. At each trial site, community organizations should advocate for the establishment of a community advisory board (CAB).
3. At each trial site, trial organizers should help facilitate the establishment of a CAB. This should include: (a) providing the CABs with adequate training and resources to carry out their functions of advising organizers, educating target communities and maintaining links with local prevention and health services; and (b) preparing materials to educate CAB members on their role.
4. Trial organizers should involve people living with HIV/AIDS in the design and implementation of vaccine trials.

The information in this series of info sheets is taken from *HIV Vaccines in Canada: Legal and Ethical Issues: An Overview*, prepared by the Canadian HIV/AIDS Legal Network. Copies of the paper and info sheets are available on the Network website at www.aidslaw.ca/Maincontent/issues/vaccines.htm and through the Canadian HIV/AIDS Clearinghouse (www.clearinghouse.cpha.ca). Reproduction is encouraged, but copies may not be sold, and the Canadian HIV/AIDS Legal Network must be cited as the source of this information. For further information, contact the Network at info@aidslaw.ca. **Ce feuillet d'information est également disponible en français.**

Funded by Health Canada, under the Canadian Strategy on HIV/AIDS. The views expressed are those of the author and do not necessarily reflect the views or policies of the Minister of Health.

Clinical Trials and the Informed-Consent Process

This info sheet defines informed consent as it applies to participating in a clinical trial; describes what information needs to be disclosed as part of the informed-consent process; and discusses how to ensure that the consent obtained is truly informed.

This is one of a series of 8 info sheets on HIV Vaccines in Canada.

CANADIAN HIV·AIDS LEGAL NETWORK | RÉSEAU JURIDIQUE CANADIEN VIH·SIDA

Canadian Strategy on HIV/AIDS

What Is Informed Consent?

In the context of a clinical trial, informed consent is the process whereby potential participants are provided with relevant information about the trial and decide about whether to participate in the trial. The concept of informed consent is grounded in the fundamental human right of individuals to control what is done to their own bodies. In Canada, informed consent is required by law for any clinical trial that involves the administration of a vaccine or any other experimental medicine. In the informed-consent process, individuals must understand the information provided and its implications for their health, and must make a voluntary, uncoerced decision about whether or not to participate in the trial.

Potential participants should be partners in the informed-consent process. Ideally, informed consent will take the form of a dialogue between the researcher and the participant in which the participant feels free to ask questions.

Information That Should Be Disclosed As Part of the Informed-Consent Process

Before potential participants decide whether to participate in a trial, they should be provided with information on:

- the benefits of participating in the trial;
- the risks of participating in the trial;
- the results from prior research;
- the objectives of the trial;
- the research hypothesis (ie, how the researchers think the candidate vaccine might work to achieve efficacy);
- the research methodologies;
- administrative details of the trial, including the identities of the sponsor, its parent corporation (if applicable), and the principal or site investigator;
- any conflicts of interest linking these parties;
- the role of the principal or site investigator;
- the obligations of the trial organizers (see info sheet 5); and
- the obligations of participants (eg, nature and frequency of appointments and tests).

With respect to the risks of participating in the trial, the nature, magnitude, and probability of all known potential harms (even those that may be considered rare or remote) must be spelled out as fully as possible.

Potential participants also need to be informed about the importance of maintaining safer behaviours to avoid contracting HIV infection throughout the trial. The experimental nature of vaccine trials

and the uncertainties concerning the efficacy of the candidate vaccine should be stressed.

The obligation to provide extensive disclosure pertains not only to information available at the outset of the trial, but also to any new information that may emerge during the course of the trial that could influence a participant's decision to continue taking part (eg, a revelation that the vaccine causes serious side effects).

The Need to Ensure That Consent Is Truly Informed

Trial organizers have an obligation not only to disclose all pertinent information but also to ensure that the consent is truly informed. This means that organizers must take all reasonable steps to ensure that potential participants understand the information about the trial and appreciate the nature, benefits, and risks of the experiment to which they are submitting. Various means can and should be used to convey the information. Possible methods include: the use of a signed consent form; interviews with the principal or site investigator and trial staff; community forums; explanatory videos; and written materials.

The choice of methods will be shaped by factors such as the culture, language, traditions, and levels of education of the target community, and the prior experience of the community with vaccine and clinical research.

The consent forms should be written in a way that makes them easily understandable and should be pre-tested on the target populations. Potential participants should have the opportunity to take the consent form and other relevant materials home to study for at least 48 hours before signing the form. Participants should be encouraged to discuss the form and the materials with their doctors, partners, families, and friends.

The use of a "participant's bill of rights" may enhance the informed-consent process. Such a bill would explicitly state the potential participant's right to free, voluntary, and informed consent; summarize the representations made by the organizers; and outline the procedures by which participants can raise questions or lodge complaints. Organizers may also want to make use of a test or other type of assessment to determine whether the potential participants understand all the relevant information about the trial (as was done in the AIDSVAX trial in Canada).

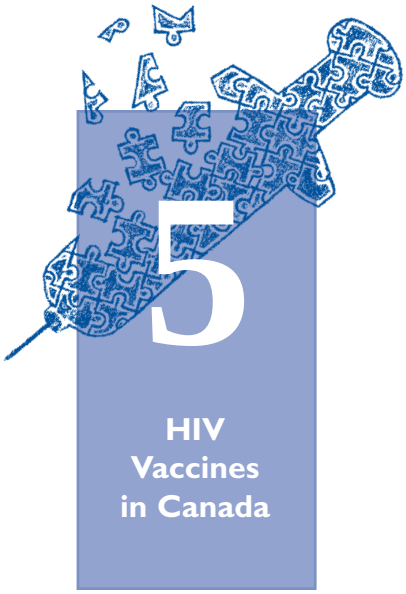
The informed-consent process needs to be adapted to different cultures. Information should be communicated in a culturally appropriate manner and in appropriate languages, which means that written materials may need to be translated or adapted.

Recommendations

1. Trial organizers should work with people from each target community to obtain input on the informed-consent process and to ensure that the process is adapted to the particular culture of that community.
2. Trial organizers should ensure that the trial protocols spell out in detail the process for obtaining informed consent, including a description of the methods that will be used to ensure that the consent is truly informed.

The information in this series of info sheets is taken from *HIV Vaccines in Canada: Legal and Ethical Issues: An Overview*, prepared by the Canadian HIV/AIDS Legal Network. Copies of the paper and info sheets are available on the Network website at www.aidslaw.ca/Maincontent/issues/vaccines.htm and through the Canadian HIV/AIDS Clearinghouse (www.clearinghouse.cpha.ca). Reproduction is encouraged, but copies may not be sold, and the Canadian HIV/AIDS Legal Network must be cited as the source of this information. For further information, contact the Network at info@aidslaw.ca. **Ce feuillet d'information est également disponible en français.**

Funded by Health Canada, under the Canadian Strategy on HIV/AIDS. The views expressed are those of the author and do not necessarily reflect the views or policies of the Minister of Health.



Obligations Toward Clinical Trial Participants

This info sheet examines three obligations that trial organizers or governments have toward participants during or after an HIV vaccine trial: the provision of preventive counselling; the provision of high-quality care to participants who become HIV-positive during the trial; and the provision of compensation to any participant who suffers a vaccine-related injury.

This is one of a series of 8 info sheets on HIV Vaccines in Canada.

CANADIAN HIV·AIDS LEGAL NETWORK | RÉSEAU JURIDIQUE CANADIEN VIH·SIDA

Canadian Strategy on HIV/AIDS

Preventive Counselling

The potential for risk behaviours among participants in an HIV vaccine trial is significant. For scientific reasons, large-scale trials often deliberately recruit populations at greater risk of contracting HIV. As well, taking part in a trial may cause participants to adopt more risky behaviours and thus expose themselves to possible infection if they prematurely or falsely assume that they are receiving the vaccine (rather than the placebo) and that the vaccine is effective. Trial organizers are therefore ethically obligated to take all reasonable actions to reduce HIV risk behaviours among participants. Preventive counselling is one way to do this.

The obligation to promote prevention starts when participants first consent to participate and continues throughout the trial. The ideal venue for doing preventive counselling is during the pre- and post-test counselling sessions that accompany the periodic HIV-antibody testing that each participant undergoes as part of the trial. However, participants should be able to request counselling sessions at any time during the trial.

Preventive counselling should be conducted by trial staff who are trained to understand the target community's culture and attitudes toward sexuality, illness, family, and injection drug use. The training could be provided by local health-care providers and AIDS service organizations who are already doing HIV-antibody testing and counselling in the community. Trial staff should take steps to update their preventive counselling skills as the trial progresses. If the midterm statistical review of results from a large-scale efficacy trial were to reveal any inordinately high levels of HIV incidence, trial staff should take steps to revise and intensify preventive interventions.

In a multi-centre trial, organizers could develop basic standards for preventive counselling to be applied at every site. However, local sites should be permitted some flexibility to adapt the standards to local conditions.

It is important to ensure that community organizations carefully monitor how well trial organizers are fulfilling their obligation to provide high-quality preventive counselling. The reason for this is that the organizers face a real dilemma. They are ethically obligated to counsel safer behaviours, but if participants do not take risks the trial will not be able to judge the efficacy of the vaccine candidate. (This is one reason why Phase III HIV vaccine trials recruit extremely large numbers of people. The expectation is that with so many people participating, even if only a very small percentage of them engage in risky behaviour, the actual numbers will

still be large enough to provide scientifically valid results concerning the efficacy of the candidate vaccine being tested.)

High-Quality Care

International ethical guidelines on the conduct of research oblige HIV vaccine trial organizers to ensure that care is provided to participants who become HIV-infected during the trial. In Canada, with its publicly funded health-care system and relative affluence, the care provided should be of the highest quality. This means that the latest drugs that have been approved for sale in Canada, including both antiretroviral medications and drugs for the treatment of opportunistic infections, should be provided. Most of these drugs are covered under provincial and territorial drug reimbursement programs, but some drugs are not covered (or are not fully covered) in some jurisdictions.

Compensation for Vaccine-Related Injury

International ethical guidelines on the conduct of research state that trial participants have a right to "equitable compensation" in the unlikely event that they suffer a vaccine-related injury as a result of participating in the trial. The rationale for this is as follows:

- Because of the non-therapeutic nature of preventive vaccine research, a volunteer in an HIV vaccine trial is acting less out of self-interest and more out of altruism than a volunteer in a clinical trial for an experimental therapy. Because participants in an HIV vaccine trial stand to gain so little, governments or industry are ethically obliged to care for them in the event of injury.
- HIV vaccine trials are critical to society's efforts to control the HIV/AIDS epidemic. To encourage people to volunteer for such trials, compensation should be provided to participants who experience adverse effects.

The guidelines state that participants should not be required to waive their right to compensation, and that the informed-consent form should not contain any wording that would absolve trial organizers from their responsibility in case of injury. The guidelines also state that participants should not be obliged to show negligence in order to claim compensation.

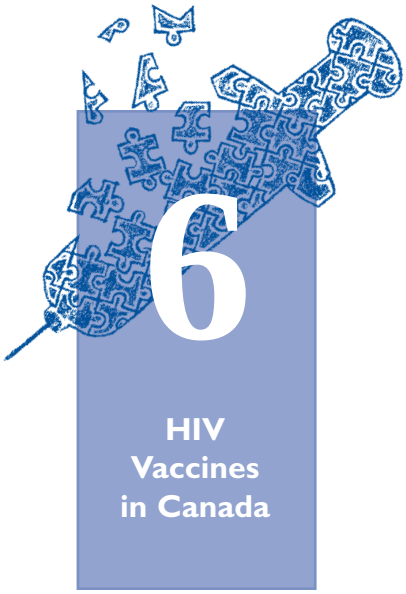
Compensation could potentially involve huge amounts of money. Profit margins tend to be much lower for vaccines than for therapeutic medications. As a result, the pharmaceutical industry is reluctant to offer compensation. So is the insurance industry. The best approach is for the federal government to institute a no-fault vaccine-related injury insurance program and for the pharmaceutical industry to contribute to the program.

Recommendations

1. Trial organizers should develop a comprehensive plan for preventive counselling prior to the start of the trial. The plan should be developed in consultation with local health-care providers and AIDS service organizations.
2. Trial organizers should ensure that the staff providing preventive counselling are knowledgeable about the cultures of the target communities.
3. Trial organizers should ensure that high-quality care and treatment is provided to any participant who becomes HIV-infected during the course of the trial. Where necessary to ensure access, organizers should subsidize the cost of any antiretroviral medications or drugs for the treatment of opportunistic infections not already covered under provincial and territorial drug reimbursement programs.
4. The federal government should establish a no-fault vaccine-related injury insurance program in Canada. The program should cover all experimental and licensed vaccines. Pharmaceutical companies should contribute to this fund.

The information in this series of info sheets is taken from *HIV Vaccines in Canada: Legal and Ethical Issues: An Overview*, prepared by the Canadian HIV/AIDS Legal Network. Copies of the paper and info sheets are available on the Network website at www.aidslaw.ca/Maincontent/issues/vaccines.htm and through the Canadian HIV/AIDS Clearinghouse (www.clearinghouse.cpha.ca). Reproduction is encouraged, but copies may not be sold, and the Canadian HIV/AIDS Legal Network must be cited as the source of this information. For further information, contact the Network at info@aidslaw.ca. **Ce feuillet d'information est également disponible en français.**

Funded by Health Canada, under the Canadian Strategy on HIV/AIDS. The views expressed are those of the author and do not necessarily reflect the views or policies of the Minister of Health.



Clinical Trials and Stigma & Discrimination

This info sheet explains why discrimination can occur as a result of participating in an HIV vaccine trial; describes how the discrimination can manifest itself; and discusses one particular form of potential discrimination – denial of insurance coverage.

This is one of a series of 8 info sheets on HIV Vaccines in Canada.

CANADIAN HIV•AIDS LEGAL NETWORK | RÉSEAU JURIDIQUE CANADIEN VIH•SIDA

Canadian Strategy on HIV/AIDS

Why Participation in HIV Vaccine Trials Can Lead to Discrimination

Stigma and discrimination have been associated with AIDS since the start of the epidemic. People living with HIV/AIDS have been discriminated against in a variety of ways. As a result of their participation in an HIV vaccine trial, HIV-negative people may also be stigmatized or discriminated against. This can occur:

- if a volunteer's participation in an HIV vaccine trial becomes known, and people associate participation in the trial as an indication of HIV infection, probable infection, or the likelihood of becoming infected;
- if people strongly disapprove of HIV risk practices and view trial participants as people likely to engage in such practices; and
- if the trials occur in marginalized communities that already experience stigma and discrimination, and the research process and its attendant publicity identify these communities and exacerbate the stigma.

Types of Discrimination

For the most part, HIV-negative participants would be subject to the same kinds of discrimination as people living with HIV/AIDS – such as harassment, denial of housing, refusal of service, loss of employment or denial of a promotion, and denial of insurance.

With respect to the workplace, there is no requirement for participants in an HIV vaccine trial to divulge their participation to their employers. But word can nevertheless get around. One way to help preserve the confidentiality of this information would be for trial organizers to ensure that participants are able to make trial-related appointments outside their normal working hours.

Participants could also be stigmatized within their own communities. Research shows that potential recruits fear unfavourable social reaction to their involvement in HIV vaccine research and consider this to be a primary risk associated with participation in a vaccine trial.

Insurance Coverage

Trial participants may be discriminated against when they apply for insurance coverage.

With some HIV vaccines, some HIV-negative participants may falsely test positive on the quick-standard HIV-antibody tests that are used. That is, the HIV test may come back positive when the individual is actually HIV-negative. This can happen because the tests are picking up the presence of

antibodies against the vaccine, as opposed to antibodies against HIV disease.

Under Canadian law, insurance companies are legally entitled to deny insurance to anyone who has a "pre-existing condition" such as HIV infection. If a trial participant applied for insurance and needed to take an HIV-antibody test as part of the application process, coverage could be wrongly denied if the insurance company incorrectly interpreted the applicant's test result as being indicative of HIV infection.

However, there are special tests available that can distinguish between a vaccine-elicited immune response and an immune response that is due to infection from HIV. These special tests are used at the antibody-testing sites established or used by HIV vaccine trials in the event that the quick-standard test produces a positive result. (Otherwise, the organizers would not know how to interpret the results of the trial.) Unfortunately, insurance companies are not legally compelled to use the testing facilities of the vaccine trial or to accept its test results. In order to protect against possible discrimination, trial organizers should:

- educate insurance companies about this issue;
- encourage insurance companies to use the HIV-antibody testing sites where the special tests are available; and
- ensure that access to sites where the special tests are available continues even after the trial ends.

In addition, insurance companies may discriminate against trial participants because the participants may be deemed "high risk" because of their participation in the trial. This is the most important issue that needs to be addressed with the insurance industry, in order to ensure that people who participate in HIV vaccine clinical trials can do so without risk of discrimination by insurance companies.

Finally, it would be helpful if trial participants were provided with documentation, such as an identification card, that shows that they are participating in an HIV vaccine trial. The identification card should contain a phone number where participants can obtain assistance if they experience discrimination.

Recommendations

1. Trial organizers should ensure that during the informed-consent process potential participants are provided with full information on the types of stigma and discrimination that could result from their participation in an HIV vaccine trial.
2. Trial organizers should ensure that support is provided to people who experience discrimination during the course of an HIV vaccine trial.
3. Trial organizers should ensure that appointment hours are flexible enough to allow participants to attend appointments outside the participants' working hours.
4. Trial organizers should provide participants with documentation that shows they are taking part in an HIV vaccine trial. This could take the form of an identification card. The card should include a phone number that participants can call in the event they experience discrimination related to their involvement in the trial.
5. When testing candidate vaccines that can produce a false positive result on an HIV-antibody test, trial organizers should educate insurance companies about the issue; encourage insurance companies to use the HIV-antibody testing sites where special tests are available that can distinguish between a vaccine-elicited immune response and an immune response that is due to infection from HIV; and ensure that access to the sites where special tests are available continues after the trial ends.
6. The insurance industry shall not discriminate against trial participants simply because of their participation in an HIV vaccine trial.

The information in this series of info sheets is taken from *HIV Vaccines in Canada: Legal and Ethical Issues: An Overview*, prepared by the Canadian HIV/AIDS Legal Network. Copies of the paper and info sheets are available on the Network website at www.aidslaw.ca/Maincontent/issues/vaccines.htm and through the Canadian HIV/AIDS Clearinghouse (www.clearinghouse.cpha.ca). Reproduction is encouraged, but copies may not be sold, and the Canadian HIV/AIDS Legal Network must be cited as the source of this information. For further information, contact the Network at info@aidslaw.ca. **Ce feuillet d'information est également disponible en français.**

Funded by Health Canada, under the Canadian Strategy on HIV/AIDS. The views expressed are those of the author and do not necessarily reflect the views or policies of the Minister of Health.

Planning Now for Vaccine Delivery

This info sheet explains why Canada needs to start now to develop a formal HIV vaccine delivery plan; describes what should be included in such a plan; and discusses potential obstacles to HIV vaccine delivery.

This is one of a series of 8 info sheets on HIV Vaccines in Canada.

CANADIAN HIV·AIDS LEGAL NETWORK | RÉSEAU JURIDIQUE CANADIEN VIH·SIDA

Canadian Strategy on HIV/AIDS

The Need for a Vaccine Delivery Plan

Discovery of an HIV vaccine will not automatically lead to effective delivery of that vaccine to the people most at risk of HIV infection. Experience with other vaccines in Canada reveals many instances of less than optimal coverage. One example of this is the delivery of hepatitis A and B vaccines to gay and bisexual men - the risk of infection is fairly high but the proportion of men who have received the full series of vaccinations for both diseases remains relatively low. One cohort study among gay and bisexual men in Montréal revealed hepatitis B vaccination rates of 49 percent, of which only three-fifths had received all three inoculations required; and hepatitis A vaccination rates of 38 percent, of which less than three in ten had received both inoculations required.

It is not possible to predict exactly when an HIV vaccine will be available. However, it is not unreasonable to expect that a low-efficacy vaccine could be on the market as soon as a few years from now, and that a higher-efficacy vaccine could become available not too many years after that. Even a low-efficacy vaccine could be a useful addition to the existing arsenal of prevention strategies. Therefore, Canada needs to be prepared for the day when a vaccine is ready to be delivered. Given the complexities of vaccine delivery, Canada needs an HIV vaccine delivery plan. Health Canada should start immediately to coordinate the development of such a plan. If we wait any longer, useful HIV vaccines will almost certainly emerge without Canada having a strategy in place to get the vaccine to the people who most need protection from the virus.

What an HIV Vaccine Delivery Plan Should Contain

Initially, the plan will have to be fairly general. It will not be possible to develop detailed strategies until more is known about the characteristics of the vaccine that will be delivered – characteristics such as effectiveness, duration of protection, number of doses required, and method of delivery. However, it is now possible to develop the broad outlines of a delivery plan. The plan should provide answers to questions such as: Who will be vaccinated and under what conditions? How will vaccine delivery be financed? How will Canada ensure that there is a sufficient supply of the vaccine? How will the vaccine be distributed? What measures will be required to encourage the highest possible levels of vaccine uptake? What strategies will be required to ensure that coverage remains at a high level if multiple doses need to be administered over a long period of time? Who will coordinate vaccine delivery and what will the roles and responsibilities of key

players be? If a limited supply of the vaccine is available, what criteria will be used to determine what delivery strategies should be employed or which communities should be prioritized? What measures need to be put in place to ensure that any vaccine-induced adverse events are promptly identified and reported? How will issues of liability be handled? How will individuals be compensated for vaccine-induced adverse events? What measures need to be put in place to protect those who have been vaccinated from discrimination? What monitoring and evaluation systems need to be developed? How will communities be informed and educated about the availability of a preventive HIV vaccine? How will other HIV-prevention strategies be incorporated into the delivery of an HIV vaccine?

The plan should include hypothetical delivery models based on different scenarios of vaccine efficacy (eg: How we might use a 30 percent versus a 90 percent efficacy vaccine). It should consider using a variety of settings to deliver the vaccine, in addition to physicians' offices and community health clinics (eg, pharmacies, workplaces, schools, family planning clinics, needle exchange sites, community centres, gay pride events).

Inoculation with a vaccine that offers less than complete protection against infection – and particularly with a comparatively low-efficacy vaccine – might actually increase HIV incidence if the inoculation program led people who are vaccinated (or others in the community) to relax their safer sex and needle sharing practices. It will be critical, therefore, to ensure that people are counselled to maintain risk-reduction behaviours. The plan needs to spell out how this will be done.

Given current HIV vaccine research patterns, it is quite possible that an effective HIV vaccine will emerge from a trial conducted in just one or two target communities. Therefore, the vaccine delivery plan will need to provide for "bridging studies" that could rapidly be mounted to determine whether the vaccine is effective in other communities.

A Canadian HIV vaccine delivery plan must also take into account the global dimensions of the epidemic. In order to reap the greatest possible public health benefit, a national strategy for domestic delivery will need to be firmly anchored in a global delivery strategy.

Potential Obstacles to Delivery

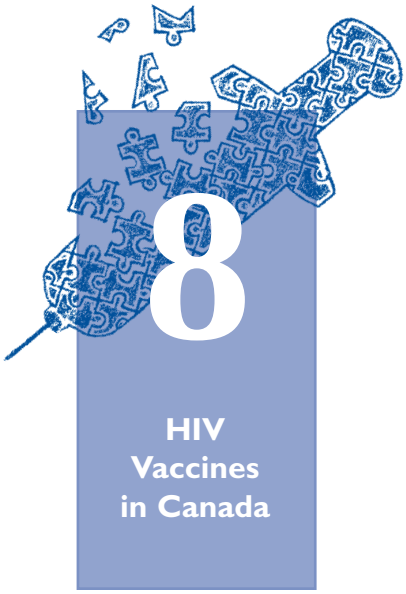
Potential obstacles to the delivery of an HIV vaccine include: scepticism and distrust of vaccines generally; the possibility that people will underestimate the risks and consequences of HIV infection; and potential discrimination against those who are vaccinated. To overcome these obstacles, and to achieve the degree of public confidence and support needed to ensure a high level of vaccine coverage, the case for HIV vaccination will need to be presented in a manner that clearly outlines the potential benefits and risks both for individuals and for public health.

Recommendations

1. As part of the Canadian HIV Vaccine Plan, Health Canada should immediately begin to coordinate the development of a plan for the delivery of an HIV vaccine. The delivery plan should be developed in consultation with the provincial and territorial governments, health-care providers, public health officials, organizations representing target communities, and other stakeholders. Once it has been developed, the plan should be updated regularly to reflect the latest developments in HIV vaccine research.
2. Public health officials and affected communities should work together to advocate for vaccine delivery in those communities where it is most needed.
3. Prior to implementing a vaccine delivery plan, governments should ensure that the target communities are provided with clear and comprehensive information about the benefits, efficacy, safety, and risks of the HIV vaccine; and information on the risks of not being vaccinated.

The information in this series of info sheets is taken from *HIV Vaccines in Canada: Legal and Ethical Issues: An Overview*, prepared by the Canadian HIV/AIDS Legal Network. Copies of the paper and info sheets are available on the Network website at www.aidslaw.ca/Maincontent/issues/vaccines.htm and through the Canadian HIV/AIDS Clearinghouse (www.clearinghouse.cpha.ca). Reproduction is encouraged, but copies may not be sold, and the Canadian HIV/AIDS Legal Network must be cited as the source of this information. For further information, contact the Network at info@aidslaw.ca. **Ce feuillet d'information est également disponible en français.**

Funded by Health Canada, under the Canadian Strategy on HIV/AIDS. The views expressed are those of the author and do not necessarily reflect the views or policies of the Minister of Health.



Essential Resources

This info sheet lists a number of resources related to HIV vaccines. It provides information on the papers on which this series of info sheets is based, on publications that deal with the ethics of research, on publications by NGOs that deal with HIV vaccine issues, on other related publications, and on selected journal articles and websites.

This is one of a series of 8 info sheets on HIV Vaccines in Canada.

1. Current State of HIV Vaccine Research
2. Why We Need a Canadian HIV Vaccine Plan
3. Involving Communities in the Conduct of Clinical Trials
4. Clinical Trials and the Informed-Consent Process
5. Obligations Toward Clinical Trial Participants
6. Clinical Trials and Stigma & Discrimination
7. Planning Now for Vaccine Delivery
8. Essential Resources

CANADIAN HIV•AIDS LEGAL NETWORK | RÉSEAU JURIDIQUE CANADIEN VIH•SIDA

Canadian Strategy on HIV/AIDS

Overview and Background Paper

This series of info sheets has been adapted from *HIV Vaccines in Canada: Legal and Ethical Issues – An Overview*, prepared by the Canadian HIV/AIDS Legal Network. Copies of the overview and info sheets are available in English and French on the Network website at www.aidslaw.ca/Maincontent/issues/vaccines.htm and through the Canadian HIV/AIDS Clearinghouse (www.clearinghouse.cpha.ca).

The overview itself was based on *HIV/AIDS and Vaccines: Legal and Ethical Issues – A Backgrounder*, prepared by David Thompson for the Canadian HIV/AIDS Legal Network. Copies of the background paper (in English only) are available on the website of the Network at www.aidslaw.ca/Maincontent/issues/vaccines.htm.

Publications on Ethical Issues in Research

The following publications provide useful ethical guidance for the conduct of HIV vaccine research and other research involving human subjects.

Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization. *International Ethical Guidelines for Biomedical Research Involving Human Subjects*. Geneva: 1993. See also the revised January 2002 draft of these guidelines. Available on the website of the Council (www.cioms.ch).

Joint United Nations Programme on AIDS (UNAIDS). *Ethical considerations in HIV preventive vaccine research*. Geneva: May 2000. This UNAIDS Guidance Document is available on the website of UNAIDS (www.unaids.org).

Medical Research Council of Canada, National Science and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada. *Tri-Council Policy Statement: Ethical conduct for research involving humans*. August 1998. Available on the website of the National Science and Engineering Research Council of Canada (www.nserc.ca).

Publications by NGOs on HIV Vaccine Issues

Avrett S. *HIV Vaccines for Developing Countries: Advancing Research and Access*. Canadian HIV/AIDS Legal Network, 2002. Available on the website of the Network at www.aidslaw.ca/Maincontent/issues/vaccines.htm. Discusses global strategies to promote HIV vaccine research and access to an eventual HIV vaccine.

International Council of AIDS Service Organizations. *Developing Vaccines to Prevent HIV and AIDS: An Introduction for Community Groups*. July 2000. Available on the website of the Council (www.icaso.org). Explores the need for an HIV vaccine; describes the vaccine-development process; lists some ethical issues involved in HIV vaccine trials; discusses how communities can get involved.

Snow B (ed). *HIV Vaccine Handbook: Community Perspectives in Participating in Research, Advocacy and Progress*. AIDS Vaccine Advocacy Coalition. December 1999 (2nd printing). Available on the website of the Coalition (www.avac.org). Contains a series of articles. Some of the articles that relate directly to topics addressed in these info sheets are: Working with Communities; Community Advisory Boards; HIV Vaccines and Human Rights; Participants' Bill of Rights; and Social, Ethical and Political Considerations.

Other Publications

de Bruyn T. *HIV/AIDS and Discrimination: A Discussion Paper*. Canadian HIV/AIDS Legal Network and the Canadian AIDS Society, March 1998. Available on the website of the Network at www.aidslaw.ca/Maincontent/issues/discrimination.htm.

United Nations General Assembly. *Declaration of Commitment on HIV/AIDS*. June 2001. Available on the website of the Joint United Nations Programme on HIV/AIDS (www.unaids.org) under "UN Special Session on HIV/AIDS."

World Health Organization (WHO), Joint United Nations Programme on HIV/AIDS (UNAIDS). *Future Access to HIV Vaccines*. Report from a WHO–UNAIDS Consultation, Geneva, 2-3 October 2000. (Final draft, 5 February 2001). Health Technology and Pharmaceuticals, World Health Organization. Available on the website of UNAIDS (www.unaids.org) under "Publications."

Journal Articles

Emmanuel EJ et al. What makes clinical research ethical? *Journal of the American Medical Association* 24/31 May 2000; 283(20): 2701-2711.

Juengst ET. Commentary: What "Community Review" can and cannot do. *Journal of Law, Medicine & Ethics* Spring 2000; 28(1): 52-54.

Websites

www.hivnet.ubc.ca/ctn
The website of the Canadian HIV Trials Network. Contains general information on clinical trials.

www.iavi.org
The website of the International AIDS Vaccine Initiative. Contains information on HIV vaccines and efforts to accelerate HIV vaccine research.

www.vaxgen.com/vaccine
The website of VaxGen, the manufacturers of AIDSVAX B/B, a vaccine currently being tested in large-scale efficacy trials in Canada, the United States, and the Netherlands; and AIDSVAX B/E, currently undergoing testing in Thailand. Contains information on the AIDSVAX trials.

www.who.int/HIV-vaccines
The website of the WHO–UNAIDS HIV Vaccine Initiative.

www.niaid.nih.gov/vrc/
The website of the Vaccine Research Center at the (US) National Institutes of Health.

www.avac.org
The website of the AIDS Vaccine Advocacy Coalition.

For More Resources...

contact the Resource Centre of the Canadian HIV/AIDS Legal Network: www.aidslaw.ca/maincontent.htm#rc.

The information in this series of info sheets is taken from *HIV Vaccines in Canada: Legal and Ethical Issues: An Overview*, prepared by the Canadian HIV/AIDS Legal Network. Copies of the paper and info sheets are available on the Network website at www.aidslaw.ca/Maincontent/issues/vaccines.htm and through the Canadian HIV/AIDS Clearinghouse (www.clearinghouse.cpha.ca). Reproduction is encouraged, but copies may not be sold, and the Canadian HIV/AIDS Legal Network must be cited as the source of this information. For further information, contact the Network at info@aidslaw.ca. **Ce feuillet d'information est également disponible en français.**

Funded by Health Canada, under the Canadian Strategy on HIV/AIDS. The views expressed are those of the author and do not necessarily reflect the views or policies of the Minister of Health.