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Canadian Microbicides Action Plan

**Prepared for the
Canadian Microbicides Action Plan Steering Committee**

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Disclaimers

Mention of specific products in development, or of specific organizations or corporations, does not constitute endorsement.

Summary Document

An abridged version of the Canadian Microbicides Action Plan is available as a separate document.

Acronyms

AIDS	Acquired Immune Deficiency Syndrome
AMAG	African Microbicides Advocacy Group
ARV	Anti-Retroviral treatment
ASO	AIDS Service Organization
CAB	Community Advisory Board
CAS	Canadian AIDS Society
CBO	Community-Based Organization
CIDPC	Centre for Infectious Disease Prevention and Control
CIHR	Canadian Institutes of Health Research
CMAP	Canadian Microbicides Action Plan
CSC	Correctional Service Canada
FNIHB	First Nations and Inuit Health Branch, Health Canada
GCM	Global Campaign for Microbicides
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
ICAD	Interagency Coalition on AIDS and Development
IDU	Injection Drug User or People who Inject Drugs
IPM	International Partnership for Microbicides
IRMA	International Rectal Microbicide Advocates
MAG-Net	Microbicide Advocacy Group Network
MDG	Millennium Development Goal
MDS	Microbicide Development Strategy
MSM	Men who have Sex with Men
NGO	Non-Governmental Organization
PHA	People Living with HIV/AIDS
PHAC	Public Health Agency of Canada
R&D	Research and Development
STI	Sexually Transmitted Infection
UNAIDS	United Nations Joint Program on HIV/AIDS
UNGASS	United Nations General Assembly Special Session on HIV/AIDS

A Call for Action

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

“The idea that women will have a way of re-asserting control over their own sexuality, the idea that they will be able to defend their bodily health, the idea that women will have a course of prevention to follow which results in saving their lives, the idea that women may have a microbicide which prevents infection but allows for conception, the idea that women can use microbicides without bowing to male dictates --- indeed the idea that men will not even know the microbicide is in use...these are ideas whose time has come.”

Speech delivered by Stephen Lewis, the UN Secretary-General's Special Envoy for HIV/AIDS in Africa, to the Microbicides 2004 conference in London.

Vision

Canada will contribute to global efforts to develop safe and effective microbicides that are globally accessible, both in Canada and around the world, for the prevention of HIV and other sexually transmitted infections.

Purpose of this Plan

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

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

Values

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

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

Human Rights. Every person – regardless of factors such as sexual orientation, race, culture, gender, risk behaviour or socio-economic status – has the right to health and to the highest standard of affordable and accessible prevention, treatment and care, including with respect to their sexual and reproductive health. Important aspects of a human rights based approach include²:

- An emphasis on participation of individuals and communities in decisions affecting their rights
- The universality of rights, in that they are intended to be enjoyed by everyone without discrimination
- The responsibility of States to transfer the benefits of scientific progress and its applications³
- The concept of progressive realization of the right to health
- The centrality of the role of States in assuring the public health and addressing epidemic diseases⁴

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

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

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

A Multi-Sectoral Approach. Canada will use a multi-sectoral approach that involves all levels of government, researchers, the community and the private sector to fulfill its role in microbicides development and distribution and make full use of its expertise.

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

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

² Canadian HIV/AIDS Legal Network (2005). *HIV Treatments, Vaccines and Microbicides: Developing an Agenda for Action*. Background Paper.

³ International Covenant on Economic, Social and Cultural Rights Article 15(b).

⁴ D Patterson. *Resolving Legal, Ethical and Human Rights Challenges in HIV Vaccine Research*. Canadian HIV/AIDS Legal Network, 2000: www.aidslaw.ca/durban2000/vaccinefinal.pdf

Ethical Practice. All of Canada's microbicides efforts will be held to high ethical standards, including those set out in the *Ethical considerations in HIV preventive vaccine research – UNAIDS guidance document* developed by the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS), and the Global Campaign for Microbicides report *Rethinking the Ethical Roadmap for Clinical Testing of Microbicides: Report on an International Consultation*⁵.

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

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

Gender Equality. Microbicides efforts complement ongoing work to eliminate the gender inequalities that put women and girls at increased risk of HIV infection and deprive them of appropriate prevention, diagnosis, care, treatment, support and other necessary services. Achieving gender equality in relation to HIV/AIDS includes improving women and girls' access to female-controlled HIV prevention methods such as microbicides.

Universal Access. The Government of Canada endorses the goal of universal access to comprehensive HIV/AIDS prevention, treatment, care and support by 2010.

Culturally and Community Relevant Interventions. Canada's microbicides efforts at home and abroad will be respectful of communities, culturally appropriate, flexible, designed to meet the needs and circumstances of the communities they are meant to serve, and will be built in collaboration with those communities.

Protecting and Promoting Sexual and Reproductive Health and Rights. Women, men and youth have the right to control their own sexual and reproductive health. Sexual and reproductive rights refer to an individual's right to exercise control over his or her own body, sexuality and reproduction and include⁶:

- The right to attain the highest standard of sexual and reproductive health
- The right to safety and dignity
- The right to decide whether and when to have children, and how many
- Rights to information about and access to a range of sexual and reproductive health services
- The right to make decisions and exercise control over one's sexuality and reproduction free of discrimination, coercion and violence
- The right to protect one's health and to prevent disease
- The right to choose among available options
- The right to privacy and confidentiality

Informed Choice. Individuals must understand their options for promoting their own sexual and reproductive health and have the ability to weigh the pros and cons of various options. Policymakers, managers of health care programs, health care workers, and community leaders must

⁵ Global Campaign for Microbicides (March 2005). *Rethinking the Ethical Roadmap for Clinical Testing of Microbicides: Report on an International Consultation*. <<http://www.global-campaign.org/researchethics.htm>>

⁶ Engender Health (2003): *Realizing Rights in Sexual and Reproductive Health Services*. <<http://engenderhealth.org/res/offc/ic/choices/pdf/choices.pdf>>

work together to support individuals in making informed and voluntary decisions about their sexual and reproductive health.

GIPA Principle. In addition to the principles outlined above, this Action Plan adheres to the *GIPA Principle* (i.e., the Greater Involvement of People Living with or Affected by HIV/AIDS) throughout its development, its implementation and monitoring. A central principle of any action on microbicides is that people living with HIV, and in particular women living with HIV, have important input through their own lived experiences.

About the Canadian Microbicides Action Plan

The following pages set out some elements of a Canadian Microbicides Action Plan (CMAP), as well as the issues that a comprehensive plan should address. The CMAP is the first of its kind in the world; no other country has developed a multi-sectoral microbicides Action Plan to articulate domestic and global contributions.

The CMAP is the result of a collaborative process, involving researchers, government, industry and the community. During three successful Microbicides Symposia held in Canada in October 2003, March 2005 and April 2006, representatives from various sectors (government, industry, community, research) and international partners jointly identified the need for a multi-sectoral microbicides action plan to articulate domestic and global contributions from Canada. These three Microbicides Symposia were important steps in generating dialogue and taking stock of social issues and updates on research progress. The Symposia were also instrumental in providing an opportunity for networking amongst interested stakeholders, and engaging more partners in the effort. Symposium participants from government, community, industry, international partners, and research constituencies defined desired outcomes for each of their sectors and spearheaded a Steering Committee that would guide the development of the CMAP.

The Steering Committee was comprised of representatives from the following organizations and was coordinated by the Canadian AIDS Society:

- Action Canada for Population and Development
- African Canadian HIV/AIDS Capacity Building Project
- Atlantic Centre of Excellence for Women's Health
- Canadian Aboriginal AIDS Network
- Canadian African Partnership on AIDS, Canadian Physicians for AIDS and Relief
- Canadian AIDS Society
- Canadian Institutes of Health Research
- Canadian International Development Agency
- Canadian Treatment Action Council
- Health Canada - International Affairs Directorate
- Interagency Coalition on AIDS and Development
- Polydex Pharmaceuticals
- Public Health Agency of Canada – HIV/AIDS Policy, Coordination and Programs Division
- Voices of Positive Women
- Women's Health in Women's Hands

The CMAP was developed with guidance from the Steering Committee and based on document review and extensive consultation with a broad range of stakeholders in February and March 2006. Participants of the consultation interviews are listed in Appendix A.

Background

Definition

A *microbicide* is a substance that would substantially reduce transmission of HIV and perhaps other sexually transmitted infections (STIs) when applied either in the vagina or rectum. A microbicide could be produced in many forms, including gels, creams, suppositories, films, lubricants, or in the form of a sponge or a vaginal ring that slowly releases the active ingredient. The word “microbicides” refers to a range of different products that share one common characteristic: the ability to prevent the sexual transmission of HIV and other STI pathogens when applied topically.⁷

Prototype microbicides are designed to be inserted prior to each act of sexual intercourse and could also be contraceptive, although most current potential microbicides are not. Though no microbicide has yet been proven safe and effective, scientists are pursuing nearly 60 leads, including 15 products that are currently in clinical human trials.

Several phase III efficacy trials of candidate microbicides are currently in progress or will soon commence, and with sufficient investment of resources and political will, a definitive answer to their efficacy and safety is anticipated by 2010⁸. Microbicides will likely be available before an HIV vaccine, and will complement vaccines in an overall HIV/STI prevention strategy once they do exist.

HIV in the Global Context

As the AIDS epidemic enters its third decade, it has become clear that the global scale of the AIDS crisis now outstrips even the worst-case scenarios imagined a decade ago. Since the first reports of clinical evidence of HIV/AIDS in 1981, over 25 million people have died of AIDS worldwide.

UNAIDS estimates⁹ that 33.2 million [30.6–36.1 million] people are living with HIV/AIDS worldwide in 2007, of which 46.4% (15.4 million) are women. Over 6800 new HIV infections occurred globally everyday in 2007. By the end of 2007, the majority (80%) of people living with HIV/AIDS (PHAs) are still found mainly in the countries of sub-Saharan Africa and South and South-East Asia, while an estimated 2.1 million PHAs live in North America.

Enabling uninfected individuals to protect themselves from HIV, and providing adequate and affordable treatment and care to PHAs are two serious challenges facing humankind today. In some industrialized countries including Canada, 25 years of response from community stakeholders and government has helped slow the epidemic.

⁷ Fact Sheet #2: Frequently Asked Questions About Microbicides. <[http://www.global-campaign.org/clientfiles/FS2-FAQs\[E\]07.pdf](http://www.global-campaign.org/clientfiles/FS2-FAQs[E]07.pdf)>

⁸ Canadian AIDS Society, *Community Mobilization Kit for Microbicides*, (2004). <<http://www.cdnaids.ca/web/repguide.nsf/pages/cas-rep-0006>>

⁹ UNAIDS. AIDS Epidemic Update. December 2007. <http://data.unaids.org/pub/EpiReport/2007/2007_EpiUpdate_en.pdf>

However, the prospect of rebounding against the HIV/AIDS epidemic has been hampered in some countries by public and government complacency and stalled prevention efforts that do not reflect the evolution of the epidemic. There is growing evidence that an overlap of inequalities based on health, income, gender, sexuality, ethnicity and age contribute to rising HIV cases even within developed countries, where the greatest proportions of the new infections are in low-income, marginalized communities. Effective prevention and treatment efforts need to be pursued further¹⁰, including male and female condoms, STI testing and treatment, voluntary testing and counseling, prevention of mother to child transmission, and harm reduction measures such as needle exchanges, safe injection facilities and methadone maintenance programs. A microbicide, even if only partially effective, would be one of these prevention techniques.

Globally, the HIV/AIDS epidemic is increasingly affecting women. The majority of HIV-infected women live in the countries of sub-Saharan Africa, where heterosexual transmission remains the predominant mode of HIV transmission within the adult population. Women have limited options to protect themselves and are often unable to negotiate condom use. Poverty, gender inequality, and fear of abuse and abandonment often constrain or nullify women's abilities to negotiate safer sex. Cultural attitudes and religious values can further limit the ability of women to protect themselves from HIV. Where sex is sold, there often are economic incentives for practicing unprotected sexual intercourse. In addition, women are biologically eight times more likely to become infected with HIV through vaginal intercourse than are their male partners.¹¹

HIV in the Canadian Context

Although HIV infections in Canada are relatively low from a global perspective, it is estimated that 58,000 people were living with HIV/AIDS in Canada at the end of 2005.¹² These numbers are significant relative to Canada's population of approximately 32 million. Despite evidence that Canadians generally have a good understanding of modes of HIV transmission, risk factors and prevention options, the virus continues to spread. About 4,000 new infections occur each year across an increasingly wide range of subgroups in Canada.

Prevention initiatives, including needle and syringe exchange, methadone maintenance therapy, and safer sex education, have helped slow the spread of the infection in many contexts, but are not uniformly available to all Canadians. Many of those most at risk for HIV infection face multiple barriers to accessing services, tend to be on the margins of society and are difficult to reach with prevention messages. Unfortunately, stigma, marginalization, prejudice and discrimination continue to go hand-in-hand with HIV/AIDS.¹³

Population-Specific Issues

In the Canadian context, the creation of microbicides will have a positive impact on many populations. All population-specific efforts should be guided by a social justice approach which aims to reduce oppression of those who are marginalized in our society.

¹⁰ J. Godwin, *HIV treatments, Vaccines and Microbicides. Developing an Agenda for Action: A Discussion Paper*, Canadian HIV/AIDS Legal Network, November 2003. <<http://www.aidslaw.ca>>

¹¹ WHO Fact Sheet No 242 *Women and HIV/AIDS*, June 2000. <<http://www.who.int>>.

¹² Public Health Agency of Canada, *Estimates of the Number of People Living with HIV in Canada, 2005*. <http://www.phac-aspc.gc.ca/media/nr-rp/2006/20060731-hiv-vih_e.html>

¹³ HIV/AIDS Stigma and Discrimination: A Discussion Paper, March 1998. <<http://www.aidslaw.ca>>.

In Canada, people living with or affected by HIV/AIDS experience an intersection of racism, sexism, homophobia, and general fear of HIV/AIDS. HIV prevention efforts, including efforts to develop and deliver microbicides, need to be mindful and aware of the impact of oppression and marginalization with regard to gender, age, disability, colour, social class, race, religion, language, political beliefs or sexual orientation. This anti-oppression approach is applied below to specific population groups.

Women

HIV infections among women in Canada are rising. In 2006, women constituted more than one quarter of all new HIV cases.¹⁴ Amongst these women, HIV rates are highest among Canadian women aged 15 to 29 years. In 2003/04, this group accounted for 42.5% of HIV-positive reports among women.¹⁵ At the same time, older women in Canada (aged 40 to 49 years) are increasingly at risk of contracting HIV. Women of this age group constituted 23% of HIV reports in adult females by 2002.¹⁶ According to Health Canada, heterosexual contact and intravenous drug use are the main causes of HIV transmission in women.

Because of female biology, women are at greater risk of contracting HIV through unprotected heterosexual sex because HIV is transmitted eight times more efficiently from men to women, than from women to men. Women have a much larger area of skin and tissue that is exposed to their partner's secretions during sex than men. Additionally, HIV-infected semen has a higher concentration of the virus than vaginal secretions. It should also be noted that women also engage in anal sex and thus rectal microbicides would be of value for women as well as men who have sex with men.

Women also often have limited control over safer sex decisions as women can be socially and/or economically dependent on partners, limiting their power to negotiate condom use. A microbicide that is odourless and tasteless will be especially beneficial to women as they will be able to take more control over protecting themselves. Efforts to promote microbicides and a women's right to sexual self-determination should go hand in hand. In addition, many products currently in trials could provide protection against STIs. Not only will microbicides prevent HIV or STI re-infection, but also the benefits of microbicides will be bi-directional, protecting both partners. Some microbicides may also have contraceptive properties. Microbicides may also provide an option of skin-to-skin intimacy and could be pleasure enhancing.

Microbicides could be of value to women who are victims of sexual coercion such as in the contexts of marital rape, common-law rape, or other long-term sexual violence where women have little control over their reproductive and sexual health. Microbicides may offer a strategic tool for women trying to mitigate the negative impact of sexual violence¹⁷.

Women who have sex with women may also benefit from future microbicides. Though more research is needed to understand HIV transmission among lesbian women, there is the potential of STI transmission between lesbian women through shared sex toys.

¹⁴ Public Health Agency of Canada. *HIV/AIDS Epi Updates, August 2006*, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2006: 5.

¹⁵ Health Canada, *HIV/AIDS EPI Updates, April 2003*, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Health Canada, 2003: 2.

¹⁶ Health Canada, *HIV/AIDS EPI Updates, April 2003*, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Health Canada, 2003: 2.

¹⁷ Women's Health in Women's Hands (2006). *Silent Voices, Stigma Study*.

<<http://www.whiwh.com/Silent%20Voices%20of%20HIV%20Final%20Report.pdf>>

Men

Men accounted for 73% of new infections overall in Canada in 2006¹⁸ and men who have sex with men (MSM) accounted for 40% of new infections.¹⁹ Gay men and MSM continue to account for the largest number of new infections in Canada. In 2002 they represented 58% of all PHAs.²⁰ This population also had the largest increase in infections, up 10% since 1999.

It should be noted that microbicides will provide bi-directional protection, protecting both partners during sex. Men, like women, report low levels of condom use in long-term partnerships. Worldwide, men tend to have more sex partners than women, which often include extramarital partners.²¹ The risk of contracting HIV thereby increases for them and their partners.²² Secrecy and stigma may stifle discussion about HIV within couples. There seems to be a widespread misconception that microbicides will not benefit heterosexual men or men who do not engage in anal intercourse, but an important advocacy message is that microbicides will benefit men, including heterosexual men, gay men and men who have sex with men.

Without men's commitment to microbicides and safer sex, successful HIV prevention is not feasible. This is especially true given that existing research suggests that women in many countries will not feel comfortable using microbicides without discussions with their male partner. Research conducted among men in the United States, Zimbabwe and Mexico revealed that Zimbabwean men were likely to demand that their female partners inform them if they were using a microbicide product. Mexican respondents stated if the microbicides acted as a contraceptive, it would be necessary for a woman to get her husband's consent. American men said that as long as a microbicide were safe, it would be the woman's decision whether or not to use it, although some indicated that they would still appreciate their partners telling them.²³ Many men surveyed in all three countries emphasized the importance of microbicides safety.

The complexity of sexual decision making for some gay men highlights the need for more targeted prevention information and tools such as microbicides to support safer sex. Recent Canadian data on risk behaviors suggest that MSM continue to be at elevated risk of contracting HIV and other STIs by engaging in unprotected anal and oral intercourse with casual partners.²⁴ Among other factors, complacency towards HIV infection may have risen because of lack of direct experience of the AIDS epidemic among younger gay and bisexual men,²⁵ and a desire to escape a lifetime of rigorous safer sex.²⁶

¹⁸ Public Health Agency of Canada. *HIV/AIDS Epi Updates, August 2006*, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2006: 5.

¹⁹ Public Health Agency of Canada. *HIV and AIDS in Canada. Surveillance Report to December 31, 2006*. Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2007: 17.

²⁰ Health Canada, *HIV/AIDS EPI Updates*, April 2003, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Health Canada, 2003

²¹ UNAIDS, *Men and AIDS - A Gendered Approach*, World AIDS Campaign, 2000, <<http://www.unaids.org>>.

²² *ibid* 22.

²³ C. Coggins, K. Balnchard, B. Friedland, "Men's Attitudes towards a Potential Vaginal Microbicide in Zimbabwe, Mexico and the USA," *Reproductive Health Matters*, 8(15), May 2000: 136.

²⁴ Health Canada, *HIV/AIDS EPI Updates*, April 2003, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Health Canada, 2003.

²⁵ M. Katz, "AIDS Epidemic in San Francisco Among Men Who Report Sex With Men: Successes and Challenges of HIV Prevention," *Journal of Acquired Immune Deficiency Syndromes Human Retrovirology*, 14, 1997, (Suppl 2) S38-46.

²⁶ D. Ostrow and D. McKirnan, "Prevention of Substance-Related High-Risk Sexual Behavior Among Gay Men: Critical Review of the Literature and Proposed Harm Reduction Approach," *Journal of Gay and Lesbian Medical Association*, 1(2), 1997: 97-110.

The public debate over "bare backing" amongst MSM highlights the fact that one tool (i.e., male condoms) for disease prevention is insufficient to effectively fight HIV. People protect themselves most effectively when they have a range of options from which to choose. Microbicides could thus offer an alternative to the current "condom versus no condom" decision. In addition, microbicides will allow skin-to-skin contact, thus enhancing pleasure and intimacy.

Microbicide products that have been tested for rectal use will be an important prevention option to be used in combination with condoms. Developing a microbicide suitable for rectal use is more difficult due to the different biology of the colon and the vagina. Therefore, it is likely that a rectal microbicide will be available a few years after a vaginal microbicide.²⁷

Aboriginal People

In Canada, Aboriginal people have diverse backgrounds, reflecting their diverse histories, languages, and cultures. Approximately 1.2 million people reported having at least some Aboriginal ancestry in 2006.²⁸ In 2006, 54% of people in Canada who identified themselves as Aboriginal resided in urban centers. The deplorable extent of the health and social problems in the Aboriginal population represents a human rights failure in Canada. Aboriginal people sustain a disproportionate share of the burden of physical disease and mental illness. The high incidence in the Aboriginal population of problems such as domestic violence, suicide, and alcohol abuse reflect conditions of poverty, political alienation, and racial discrimination.²⁹

Aboriginal people in Canada are also disproportionately affected by lack of access to health care, sexually transmitted infections and HIV. The surge in Canada's HIV epidemic has severely struck at Aboriginal inner-city communities. In 2006, Aboriginal people constituted over 27% of all newly reported HIV cases,³⁰ although they only represent 3.8% of Canada's total population. Poverty often impedes access to health care, and according to one study, people who died of HIV and related causes in British Columbia were more likely to be Aboriginal, female and poor.³¹ Aboriginal women make up half the total Aboriginal people living with HIV/AIDS, which is a proportion considerably higher than in the general population. Also, Aboriginal people tend to test positive for HIV infection at a younger age than non-Aboriginal people do.³²

Injection drug use remains a major mode of transmission in Aboriginal communities, with Aboriginal people who inject drugs becoming HIV-positive at twice the rate of non-Aboriginal persons who inject drugs.³³ At the same time, methadone maintenance treatment and needle exchange programs are not readily accessible for many Aboriginal people who inject drugs.

The spread of HIV amongst Aboriginal people is not only a drug-related problem; sexual transmission of HIV among Aboriginal communities is also significant. According to provincial

²⁷ Canadian AIDS Society, *Community Mobilization Kit for Microbicides*, (2004). <<http://www.cdnaids.ca/web/repguide.nsf/pages/cas-rep-0006>>

²⁸ Statistics Canada, *Aboriginal Peoples of Canada, 2006 Census*. Statistics Canada <<http://www.statcan.ca>>.

²⁹ Canadian HIV/AIDS Legal Network (1999). *Aboriginal People and HIV/AIDS: Legal Issues*. Info Sheet #2: Discrimination.

³⁰ *Public Health Agency of Canada. HIV and AIDS in Canada. Surveillance Report to December 31, 2006*. Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2007: 27.

³¹ P. Spittal, E. Wood, "Aboriginal People and the Vancouver Injection Drug Use Study", *Living Positive*, 25, July/August 2003: 32.

³² Health Canada, *HIV/AIDS EPI Updates*, April 2003, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Health Canada, 2003:37.

³³ K. Craib, P. Spittal, E. Wood et al, "Risk Factors for Elevated HIV Incidence among Aboriginal Drug Injectors in Vancouver," *Canadian Medical Association Journal*,(1) January 07, 2003: 168. <<http://www.ecmaj.ca>>.

data, in 2006, 23% of HIV cases among Aboriginal populations were attributed to heterosexual transmission while 7% of transmissions were attributed to sex between men. Injection drug use is attributed to 59% of HIV infections.³⁴

Research on the introduction of the female condom to Aboriginal communities in British Columbia demonstrates that Aboriginal women would accept a female-controlled STI prevention tool, provided that culturally appropriate support and education tools are used.³⁵ With data available from pilot projects introducing female condoms to Aboriginal communities, it is possible to surmise that broadening HIV/STI prevention options for Aboriginal people (for example, introduction of safe, easily accessible and cheap microbicides) will benefit them both on and off the reserve. Acceptability studies are critical and should be pursued and supported by funders, researchers and community groups.

Clearly, microbicides could provide an important new prevention tool for Aboriginal communities in Canada, including Aboriginal women and youth. Engaging Aboriginal communities in microbicide advocacy efforts will ensure that their needs as a community are met. The introduction of microbicides and other prevention measures should be accompanied by culturally appropriate support and education on how to use microbicides.

A microbicides information campaign that targets Aboriginal people could help raise awareness of microbicides as a possible HIV/STI protection mechanism, and increase receptivity to the use of microbicides among Aboriginal communities. Even in isolated Aboriginal communities where HIV is not viewed as a serious local problem, STIs and teenage pregnancies are high, thus pointing to the need for microbicides as one form of protection against STIs and unwanted pregnancies. Engaging Aboriginal communities in microbicides advocacy is critical to ensuring their needs are met, both in terms of product development, and marketing and delivery of an eventual product.

African and African-Caribbean Communities

In Canada, people of African and African-Caribbean descent are at particularly high risk of HIV infection.³⁶ Studies have indicated that people of African and African-Caribbean descent barriers associated with levels of English literacy, language, cultural taboos against discussing sex, homophobia, fear of the impact of a positive test on immigration status, and the lack of targeted prevention messages.

The HIV prevalence rate in the African Diaspora communities of Ontario has increased by 85% since 1996 with an average annual increase of 13%. This represents the highest increase of HIV prevalence of any exposure category.³⁷ In 2002, people of African and African-Caribbean descent

³⁴ Public Health Agency of Canada. *HIV/AIDS Epi Updates, August 2006*, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2006: 52.

³⁵ N. Marsden, S. Newmann, "The Aboriginal Female Condom Pilot Project, A Report on the Experiences of Aboriginal Women Living in Two BC Communities with the Female Condom," *BC Aboriginal AIDS Awareness Program, BC Centre for Disease Control*, 2001.

³⁶ L. Calzavara, E. Tharao, T. Myers. "Influence of immigration and country of origin on utilization of HIV-related services and programs: East African communities in Toronto," *Canadian Journal of Infectious Diseases*, 11 (Suppl. B) 2000: 64B.

³⁷ Canadian AIDS Society, *Community Mobilization Kit for Microbicides* (2004).
<<http://www.cdnaids.ca/web/repguide.nsf/pages/cas-rep-0006>>

constituted nearly 11% of all newly reported HIV cases, although they only represent 2.2% of Canada's total population.³⁸

Despite the alarmingly high death rate caused by AIDS amongst Ontario women who have immigrated from HIV endemic countries, and the high rates of maternal-infant transmission among this population, AIDS prevention initiatives and/or support programs in Canada tend to overlook African and Caribbean women. These women are at especially high risk because of cultural and religious factors, racism, discrimination and other factors that affect their capacity to negotiate safer sex, including the use of male and female condoms.³⁹ Clearly, an effective microbicide product can dramatically benefit these women. As with Aboriginal communities, the introduction of microbicides and increased awareness around prevention measures currently available should be culturally appropriate.

People Living with HIV/AIDS

Of the 58,000 people living with HIV/AIDS in Canada, more than a quarter do not know that they are HIV-positive.⁴⁰ For people living with HIV/AIDS, microbicides could help prevent other STIs, prevent reinfection with other strains of HIV and provide protection in sero-discordant couples (where one partner is HIV positive and one partner is HIV negative).

Microbicides used in combination with condoms could offer extra protection to the many men and women living with HIV/AIDS. One of the most interesting options would be a non-contraceptive microbicide that would allow protection for couples trying to conceive when one or both of them are HIV positive.⁴¹ It is important to ensure that people living with HIV/AIDS are involved in advocacy efforts and communication around microbicide creation and delivery, particularly in order to avoid stigmatizing messages against PHAs.

People who Use Drugs

The rate of HIV among persons who inject drugs in Canada remains unacceptably high, especially among Aboriginal populations.⁴² Persons who inject drugs represented 20% of people living with HIV/AIDS in 2002 and 20% of new HIV infections in 2005.⁴³

Sharing used needles creates a high risk of HIV transmission, but the link between substance use and HIV goes beyond the issue of needles. People who use alcohol, speed, crack cocaine, poppers or other non-injected drugs are at higher risk of contracting HIV than people who don't use substances. People with a history of drug use are also more likely to engage in high-risk sexual activities than people who don't use drugs.

³⁸ It should be noted that neither Ontario nor Quebec includes ethnicity information when reporting HIV positive tests despite these provinces having the highest number of new infections every year. Therefore the number of newly reported HIV infections may be different if ethnicity was reported in these two provinces. Canadian AIDS Society, *Community Mobilization Kit for Microbicides*, (2004). <<http://www.cdnaids.ca/web/repguide.nsf/pages/cas-rep-0006>>

³⁹ E. Tharao, *Would Microbicides Be Used? A perspective of African and Caribbean women in Toronto*, The Microbicides Symposium, 30 Oct 2003.

⁴⁰ Public Health Agency of Canada. *HIV/AIDS Epi Updates, August 2006*, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2006: 52.

⁴¹ Canadian AIDS Society, *Community Mobilization Kit for Microbicides*, (2004). <<http://www.cdnaids.ca/web/repguide.nsf/pages/cas-rep-0006>>

⁴² Health Canada, *HIV/AIDS EPI Updates, April 2003*, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Health Canada, 2003: 36.

⁴³ Public Health Agency of Canada. *HIV/AIDS Epi Updates, August 2006*, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2006: 75.

Existing research suggests that the sex-related and drug-related vulnerabilities faced by female persons who inject drugs may be significantly different than those faced by their male counterparts. Research has also documented the more prominent role that sexual HIV transmission may play in women who inject drugs.⁴⁴ People with a history of drug use are also more likely to engage in high-risk sexual activities.⁴⁵

High levels of alcohol consumption puts people at elevated risk of sexually transmitted HIV. The Kaiser Foundation funded a study of high-school students and alcohol use and sexual practices in the United States. The survey found that almost one quarter of sexually active young Americans aged 15 to 24 report having sex without a condom because they were drinking or using drugs at the time.⁴⁶ No similar studies have been conducted in Canada as of yet, but alcohol is often cited as the drug of choice for most Canadians.⁴⁷ It is likely that Canadian youth behave in similar fashion.

Existing approaches to HIV prevention among persons who use drugs, which include needle and syringe exchange, dissemination of harm reduction messages, opiate substitution therapy, and safe injection facilities, should be expanded. At the same time, new prevention technologies such as microbicides should be made available to prevent sexual transmission of HIV/STIs among people who use drugs. The high incidence of HIV among persons who inject drugs in Canada demonstrates that they can benefit from microbicides.

Persons who use drugs could be important beneficiaries of an additional tool for HIV/STI prevention, particularly if they have easy access to microbicides once they become available.

Prisoners

Approximately 12,000 people pass through the Canadian prison system annually.⁴⁸ Many prisoners share common histories of childhood poverty, previous incarcerations and drug or alcohol use.⁴⁹ It is estimated that the prevalence of HIV within the federal correctional environment is 10 times higher than in the Canadian population at large. Unsafe injection drug use, unsafe tattooing and unsafe sex are widespread in prisons and contribute to HIV transmission.

Condoms, lubricants and dental dams are still not universally available in prisons. Some institutions are reportedly limiting the number of condoms an inmate can possess, and in addition, "many jurisdictions have institutional regulations prohibiting consensual sex. Therefore, many sexually active prisoners will not risk calling attention to themselves by asking staff for condoms."⁵⁰ Female prisoners may be victims of sexual violence by males in correctional facilities.

High rates of Hepatitis C infection and HIV/HCV co-infection among the prison population are also attributed to unsafe injection and tattooing practices. In 1999, nearly 88% of Canadian prisoners

⁴⁴ P. Spittal, K. Craib, E. Wood, et al, "Risk factors for elevated HIV incidence rates among female injection drug users in Vancouver," *Canadian Medical Association Journal*, 166 (7) 2002: 894-9.

⁴⁵ Canadian AIDS Society, *Community Mobilization Kit for Microbicides* (2004).
<<http://www.cdnaids.ca/web/repguide.nsf/pages/cas-rep-0006>>

⁴⁶ For more information see *Sexual Activity and Substance Use Among Youth*, U.S. National Survey Conducted by the Kaiser Family Foundation, February 2002. <<http://www.kff.org>>

⁴⁷ Centre for Addiction and Mental Health, *Drugs and Alcohol, Facts and More*, <<http://www.camh.net>>.

⁴⁸ Correctional Service of Canada, *Myths and Realities: How Federal Corrections Contributes to Public Safety*, Public Works and Government Services Canada, 2002.

⁴⁹ R. Lines, *Pros & Cons: A Guide to Creating Successful Community-Based HIV/AIDS Programs for Prisoners*, PASAN, 2002: 33.

⁵⁰ R. Lines, *Pros & Cons: A Guide to Creating Successful Community-Based HIV/AIDS Programs for Prisoners*, PASAN, 2002: 66.

with HIV/HCV co-infection were exposed to the virus through injection drug use while in prison.⁵¹ At the same time, there are practically no clean needles in prisons.

For all these reasons, microbicides could be especially beneficial to inmates. The experience of making condoms and lubricants more widely available in Canadian prisons, and the ongoing struggle to make needle exchange programs available, shows that consistent community advocacy for prisoners' interests is required to ensure universal and consistent microbicides availability in prisons.

Youth

Young people aged 10 to 24 currently constitute a small group of the total number of people living with HIV/AIDS in Canada. In December 2005, youth constituted 3.5% of AIDS cases in which age was reported.⁵² The proportion of females among positive HIV test reports varies considerably by age and is highest among adolescents and young adults. In 2005 in Canada, females in the 15 to 29 year range accounted for 33.5% of all positive HIV test reports among females, a decrease from 44.5% in 2002. The limited data available about this group indicate that young women are involved in behaviours that put them at risk of contracting HIV infection.⁵³

Generally, young people are at especially high risk of HIV/STI infection due to misperceptions of their vulnerability, risky sexual behavior, and substance use. A rising incidence of chlamydia and gonorrhea among Canadian youth points to the prevalence of unprotected sexual intercourse. Biologically, young women are more vulnerable to HIV infection than are older women: the cell type covering the cervix changes as girls mature into adulthood and it becomes more impervious to microbes and other pathogens. At the same time, young women are more likely than young men not to use condoms.⁵⁴ Furthermore, youth are vulnerable to sexual violence, particularly family-based sexual violence and sexual exploitation.

The recent *Canadian Youth, Sexual Health and HIV/AIDS Study* found that alcohol use, repeated drunkenness, and student reluctance to use health services aimed at educating them about HIV/AIDS all put youth at risk.⁵⁵ One of the most alarming findings of the study was that around half of Grade 9 students surveyed believed there was a cure for AIDS. There is evidence that young Canadians tend to have multiple sexual partners, and street youth also tend to have a history of injection drug use.⁵⁶ The prevalence of HIV among young people in Canada remains low. However, data on sexual risk, STIs and substance use, combined with seemingly low concern for HIV/STI issues among Canadian youth create potential conditions for the spread of HIV within this age group. An HIV/STI prevention method that would be easy to use and that young people could control themselves would significantly reduce their vulnerability to HIV/STIs. Once microbicides become available, getting young people accustomed to using microbicides and other safer sex

⁵¹ R. Remis, *Estimating the Number of Persons Co-infected with Hepatitis C Virus and Human Immune Deficiency Virus in Canada*, Health Canada, 1999. <<http://www.he-sc.gc.ca>>.

⁵² Public Health Agency of Canada. *HIV/AIDS Epi Updates, August 2006*, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2006: 20.

⁵³ Public Health Agency of Canada. *HIV and AIDS in Canada. Surveillance Report to December 31, 2006*. Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2007: 16.

⁵⁴ Health Canada, *HIV/AIDS EPI Updates*, April 2003, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Health Canada, 2003:15.

⁵⁵ Council of Ministers of Education. *Canadian Youth, Sexual Health and HIV/AIDS Study, Factors Influencing Knowledge, Attitudes and Behaviors*, Canadian Strategy on HIV/AIDS, 2003: 52.

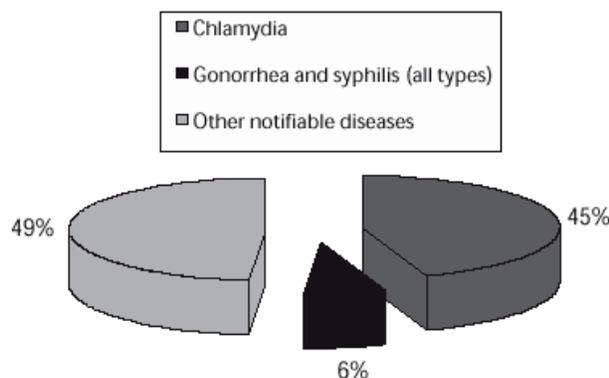
⁵⁶ E. Roy, N. Hayley, P. Leclerc, L. Cédras, J. Boivin, "HIV Incidence in the Montreal Street Youth Cohort," *Canadian Journal of Infectious Disease*, 12 (Suppl. 1) 2002: 49A.

options early on will be a key component to socializing them into safer sex practice for the rest of their lives.

Sexually Transmitted Infections (STIs)

In 1999, the World Health Organization reported the annual incidence of STIs (excluding HIV) at around 340 million cases.⁵⁷ In Australia, the United States, Canada and Western Europe, a pronounced rise in unsafe sex is triggering higher rates of sexually transmitted infections and, in some cases, a higher incidence of HIV among men who have sex with men.⁵⁸ The rising incidence of other STIs among gay men and men who have sex with men (in Amsterdam, Sydney, London, southern California, Montreal, and Vancouver for example) confirms that “more widespread risk-taking is eclipsing the safer-sex ethic promoted so effectively for much of the 1980s and 1990s.”⁵⁹ According to the United Nations Joint Program on HIV/AIDS (UNAIDS), similar trends are observed among the heterosexual populations of other countries such as the United Kingdom. This is especially the case among young people.⁶⁰

In Canada, there have been continued increases in all three nationally reportable STIs: chlamydia, gonorrhea, and infectious syphilis. This upward trend in STI rates has been reported since 1997. The rate of infectious syphilis is increasing in both males and females, but more so in males. Between 1995 and 2006, the rate of reported infectious syphilis has seen a nine-fold increase. In the same period, the rate among men has increased 11-fold. Unlike most STIs, syphilis is reported most often by men older than 30. In 2006, 86% of reported cases were found in men older than 30.⁶¹ Since 1997, outbreaks of infectious syphilis have been reported in cities across Canada, including Vancouver, Calgary, Toronto, Ottawa, and Montreal. The vast majority of these cases have been among men, mostly MSM.⁶²



As demonstrated in the figure to the left, reported cases of chlamydia comprised 45%, and gonorrhea and syphilis comprised 6%, of all notifiable diseases in Canada, 2002⁶³.

The health impact of STIs is not well recognized amongst Canadians and it is important to note that the same risk factors exist for both sexual transmission of HIV and STIs. All STIs (especially syphilis) are experiencing a very steep increase in infection rates, indicating that much more remains to be done to address sexual risk behaviours in

⁵⁷ WHO *Factsheet 110*, “Sexually Transmitted Diseases”, 2007. <<http://www.who.int/en/>>

⁵⁸ UNAIDS, *AIDS Epidemic Update*, 2001, The Body <<http://www.thebody.com>>.

⁵⁹ UNAIDS, *AIDS Epidemic Update*, 2001, The Body <<http://www.thebody.com>>

⁶⁰ UNAIDS, *AIDS Epidemic Update*, 2001, The Body <<http://www.thebody.com>>

⁶¹ Public Health Agency of Canada. *2004 Canadian Sexually Transmitted Infections Surveillance Report*, CCDR 2007;33S1: 26-27.

⁶² Public Health Agency of Canada. *2004 Canadian Sexually Transmitted Infections Surveillance Report*, CCDR 2007;33S1: 26, 29. For more detail on the outbreak in Montreal, see « Épidémie de syphilis en phase contagieuse à Montréal : Le rythme de propagation ne fléchit pas », Agence de développement de réseaux locaux de services de santé et de services sociaux, 8 mars 2004. <<http://www.santepub-mtl.qc.ca/Mi/syphilis/pdf/miseajour08032004.pdf>>

⁶³ Preliminary data: Notifiable Diseases, Surveillance and Risk Assessment Division, Public Health Agency of Canada, 2004. <<http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/05vol31/31s2/index.html>>

Canada. In Canada, young women and gay men are at higher risk for STIs and there have been some hypotheses that Canada's reductions in birth rates are due to infertility due to untreated chlamydia⁶⁴. Microbicides as a means for prevention of STIs is one aspect that will be of more interest to the mainstream population and their health service providers. With a few exceptions, patterns of STI infection related to gender have remained fairly consistent. Women continue to be disproportionately affected by chlamydia infection. Rates of gonorrhea and syphilis infection are still higher among men. For both chlamydia and gonorrhea, the males and females most at risk of infection are those between the ages of 15 and 29. The picture for syphilis, however, has changed. Among females, those most at risk continue to be between the ages of 20 and 39, whereas the males most at risk are between the ages of 25 and 59, those in the 30 to 39 age group being at greatest risk.⁶⁵

STI Rates in Canada ⁶⁶	National Goal: 50 per 100,000 by 2010				
	1997 rate	2002 rate	2004 rate	2006 rate	% change rate 2006 vs. 1997
Genital Chlamydia	113.9	179.4	200.2	202.2	78%
Gonorrhea	14.9	23.5	29.1	33.1	122%
Infectious syphilis ⁶⁷	0.4	1.5	3.5	4.6	1050%

STIs increase the likelihood of HIV transmission. Results from several studies have noted associations between HIV infection and prior STI infections. These include ulcerative STI infections in particular (syphilis and herpes), but also non-ulcerative ones (gonorrhea and chlamydia).⁶⁸ With regard to ulcerative STIs, the presence of open sores and blisters/ulcers allows for greater contact with bodily fluids and access to the bloodstream for HIV. Inflammation-causing STIs (also often referred to as "non-ulcerative STIs") increase the shedding of HIV-infected cells in the secretions of the cervix and vagina, allowing for a more efficient exchange of infectious particles.⁶⁹

Indeed, HIV infection makes people with HIV more susceptible to contracting other infections, including STIs and reproductive tract infections. To date, there has been limited integration of HIV and STI programming both in domestic contexts and internationally. Furthermore, in an HIV-infected person, STIs can be more difficult to diagnose and cure. Finally, a person living with HIV/AIDS is more likely to transmit HIV and untreated STIs in subsequent unprotected sexual contacts.

⁶⁴ National Post. Dr. Richard Grunier: "U of W must promote practising safe sex" February 10, 2006.

⁶⁵ Public Health Agency of Canada. *2004 Canadian Sexually Transmitted Infections Surveillance Report*, CCDR 2007;33S1:1-69.

⁶⁶ Data are preliminary and expected to change. Rate per 100,000 population. Population estimates provided by Statistics Canada. (Source: Statistics Canada, Demography Division, Demographic Estimates Section, July Population Estimates, 1997-2000 final intercensal estimates, 2001-2003 final postcensal estimates, 2004-2005 updated postcensal estimates, 2006 preliminary postcensal estimates.) Total population includes all provinces/territories except Saskatchewan and Nunavut, where data were not available. Source: Public Health Agency of Canada. *2004 Canadian Sexually Transmitted Infections Surveillance Report*, CCDR 2007;33S1:1-69.

⁶⁷ Infectious syphilis: primary, secondary and early latent syphilis.

⁶⁸ UNAIDS/WHO, *Consultation on STD Interventions for HIV Prevention: What Is the Evidence?* Geneva, 2000: 43.

⁶⁹ Population Council, *Sexually Transmitted Infections and HIV/AIDS*, Population Council/RTI Fact Sheets <<http://popcouncil.org>>.

Contraception

This year alone, an estimated 19 million women and girls, faced with unintended and unwanted pregnancies, will face the deadly consequences of unsafe abortion. Of the 500,000 annual maternal deaths, complications from unsafe abortion account for approximately 70,000, or 13%, of all deaths among women and girls, and hundreds of thousands of others will be left with debilitating, and frequently lifelong injuries, as a result. Over 96% of these women will come from the world's poorest nations, representing one of the widest, and most unjust, health gaps between developed and developing nations.⁷⁰

There are approximately 211 million global pregnancies annually; 87 million women become pregnant unintentionally, with approximately 46 million pregnancies ending in induced abortion. A further 31 million pregnancies miscarry or result in stillbirths. Women in all parts of the world seek to end unwanted pregnancy through abortion: of the 46 million women who choose to have an abortion each year, 78% are from developing countries and 22% are from developed countries.

In Canada, there are approximately 105,000 induced abortions per year, with 70% of those abortions in women under the age of 30⁷¹.

The causes of unplanned and unwanted pregnancy are multiple and complex:

- Gender inequality means women have less control over their own bodies
- Lack of access to family planning services and contraceptives
- Lack of information on modern contraceptive methods and reliance on traditional methods
- The failure of, or irregular use of, contraception
- Stigma surrounding single women and contraceptive use
- Lack of a woman's control over the circumstances of sexual intercourse
- Sexual violence, rape and incest
- Cultural and religious norms mean women have less power to negotiate contraception

To have full control over the spacing of children and to achieve desired family size, women and men must use, correctly and consistently, reliable contraception for the majority of a woman's fertile years. Evidence suggests that globally the number of married and unmarried women regularly using modern methods of contraception to avoid unplanned pregnancy is well below the numbers who wish to delay or better space their pregnancies.

The reasons for this are complex, ranging from ingrained social and cultural attitudes, economic circumstances and the inability of women to negotiate contraceptive use in relationships. Another reason is that in large parts of the world there is an unmet contraceptive need, and women and men simply cannot access the family planning services they want and need. Many couples are forced to rely on traditional methods which are less effective in preventing pregnancy. This inevitably leads to unplanned pregnancies.

In light of the serious issue of high rates of unwanted pregnancies, it is important that microbicides are available in both contraceptive and non-contraceptive formulations. Microbicides could provide women with a contraceptive option that will help increase their control over their reproductive health and reduce the negative impact of unwanted pregnancies.

⁷⁰ International Planned Parenthood Federation. *Death and Denial Unsafe Abortion and Poverty*. Foreword by Gareth Thomas MP, Jan 2006. Parliamentary Under-Secretary of State for International Development.

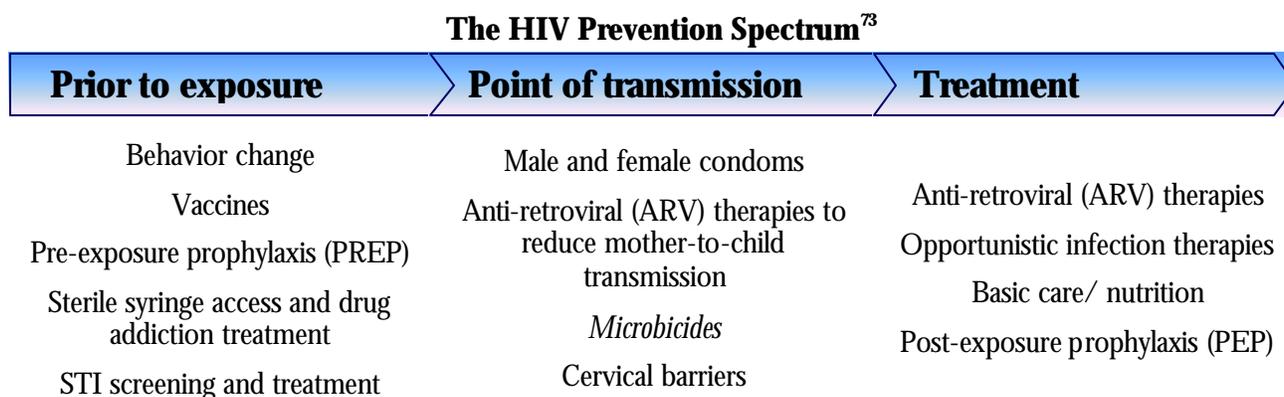
<<http://content.ippf.org/output/ORG/files/13490.pdf> >

⁷¹ Stats Can, 2006: Induced Abortions by Age Group

<<http://www40.statcan.ca/l01/cst01/health43.htm?sdi=abortions>>

Inadequacy of Currently Available Prevention Methods

No one prevention technology is sufficient to address the HIV/AIDS pandemic⁷². It is important that microbicides are conceptualized and discussed as part of what should be a full spectrum of HIV prevention options. While male and female condoms are the only technologies currently available to prevent sexual transmission of HIV, the toolbox ideally will be expanded to include other options which are proven safe and effective. In addition to microbicides, the toolbox eventually may include other cervical barriers, HIV vaccines and pre- and post-exposure prophylaxis regimens, to name a few. The following diagram illustrates how microbicides can be envisioned as fitting into the prevention spectrum.



Prevention methods for women have focused on male and female condoms, reduction in number of sexual partners and the rapid treatment of sexually transmitted infections (STIs). Using a male condom depends on the consent of the male partner and in long-term relationships its use may often be considered as a sign of infidelity and mistrust. Prevention activities that target women often fail to address effectively the risks women face in sexual relationships. In many contexts, rising rates of sexually transmitted infections indicate that abstinence and negotiating safer sex with a partner as the sole focus of prevention messages is often ineffective.⁷⁴ Empowering women to take an active role in HIV prevention through information and education, while addressing social and economic inequalities, will be more beneficial than simply settling for existing prevention methods. Enhancing the status of women is an important long-term strategy in the control of HIV. In the meantime, a microbicide would enable women to protect themselves without having to negotiate with their partner. Recognizing this in the early 1990s, advocates and scientists began calling for increased investment in HIV prevention options that could be controlled by women.

Male condoms are highly effective against HIV transmission. Some studies suggest that their effectiveness is approximately 87%, with a potential of up to 96%.⁷⁵ Despite this effectiveness, the use of male condoms is low in many settings. Lack of social and economic autonomy, cultural prohibitions and other factors make it impossible for millions of women to insist on condom use during sex. Supply and accessibility remain issues, especially in lower-income countries. According to

⁷² Global Campaign for Microbicides (2006). Fact Sheet #12: Microbicide Messaging: Themes to emphasize and avoid.

⁷³ *ibid*, 73.

⁷⁴ Health Canada, *Canadian Sexually Transmitted Diseases (STD) Epi Update*, February 2002. The Division of Sexual Health Promotion and STD Prevention and Control, Bureau of HIV/AIDS, STD and TB, Centre for Infectious Disease Prevention and Control, Health Canada.

⁷⁵ K. Davis, S. Weller, "The Effectiveness of Condoms in Reducing Heterosexual Transmission of HIV," *Family Planning Perspective*, 31, 1999: 272 – 279.

the UNFPA, current condom supplies are limited to an average of three condoms per man per year in some countries of sub-Saharan Africa.⁷⁶

The female condom, developed by a Danish doctor in the mid 1980s, added another form of physical barrier against HIV and STIs. Since 1999, UNAIDS has worked closely with the female condom manufacturer, the Female Health Company, to increase the interest of government and non-governmental agencies in female condom programs. The female condom, produced under such brand names as Reality™, Femidom™ and Femi™, has not gained desired levels of popularity for a variety of reasons, including its visibility during sex, perceived and actual difficulties with insertion, lack of usability for some women who have female genital mutilation, and cost. This is unfortunate because female condoms have their own benefits: they can be inserted up to 8 hours prior to intercourse, they are thinner than male condoms, and most importantly, they are a female initiated method of protection.

Microbicides could help fill the current prevention gap and address some of the challenges posed by current barrier methods. Other new prevention methods such as male circumcision, the HPV vaccine, HIV vaccines, and the diaphragm, are also under investigation, but results have been mixed.

Three clinical trials in sub-Saharan Africa (South Africa, Uganda and Kenya) have shown that circumcision reduces men's risk of HIV infection during vaginal sex by approximately 61%, 48% and 53% respectively. All three trials were stopped because they revealed an approximate halving of risk of HIV infection in men who were circumcised. Men in these studies received condoms, STD diagnosis and treatment, and HIV counseling. Only one trial to date has studied the impact on male-to-female transmission among HIV-positive, circumcised men and their HIV-negative female partners. The data from this trial are indeterminate. There is a possible finding that circumcision of male partners increases women's risk of acquiring HIV. This risk may be related to resuming sex before wound healing. However more information is needed, as none of these findings have been confirmed.⁷⁷ To date, there haven't been any trials assessing the impact of male circumcision on the risk of HIV transmission through anal intercourse.

There are also two trials currently underway to test the HIV prevention value of treating HSV-2 (herpes), with results expected in 2008 and 2009. The rationale for treatment of HSV-2 as a prevention method is that people infected with HSV-2 are up to three times more likely to become infected with HIV, and HSV-2 appears to accelerate HIV viral replication and shedding, making HIV more infectious. Initial large studies of herpes suppression in both HIV positive and HIV negative women from northern Tanzania involved acyclovir, an older, cheaper treatment of HSV. The HIV negative study is the first to test whether a continuous anti-herpes regimen would reduce the likelihood of contracting HIV in people already infected with genital herpes. Results were negative: among the 821 women enrolled, the rate of contracting HIV was practically the same whether they received acyclovir (400 mg twice a day) or placebo (above 4 per 100 person-years).⁷⁸

⁷⁶ UNFPA, *Promoting Reproductive Health, Saving Women's Lives*, 2001. <<http://www.unfpa.org>>

⁷⁷ A New Way to Protect Against HIV? *Understanding the Results of Male Circumcision Studies for HIV Prevention*. A Publication from the AIDS Vaccine Advocacy Coalition's *Anticipating and Understanding Results* Series. September 2007 Updated Edition
<http://aidsvaccineclearinghouse.org/pdf/MC/understanding_the_results_mc_sept.2007.pdf>

⁷⁸ The Body (September 2007). Herpes Suppression: It All Seemed So Simple.
<<http://www.thebody.com/content/treat/art43193.html>>

With respect to HIV vaccines, one Phase III HIV trial (RV144) is expected to be completed in 2008 and two phase IIB proof-of-concept trials (STEP and Phambili studies) were halted in fall 2007.⁷⁹ Based on what is presently in the development and clinical trial pipeline, scientists believe it will be six to ten years before the first HIV vaccine is licensed for use. It is important to note that this "first generation" vaccine is not likely to provide complete protection against HIV infection (what scientists call "sterilizing immunity"), but will instead slow or delay disease progression in people who receive the vaccine and later become infected with HIV. The current time estimates are influenced by a number of factors such as the scientific challenges posed by HIV; the clinical trial process, which requires large efficacy trials that take three years or more to conduct; limits on the financial resources available for vaccines discovery, for conducting Phase II and Phase III trials, and for manufacturing vaccine lots; and the need to build regulatory capacity for clinical trials and eventual product approval in many countries where trials are planned or ongoing.⁸⁰

The diaphragm is another prevention technology under study for its potential HIV prevention value. Substantial biological evidence suggests the cervix is a site of high susceptibility to HIV transmission. Researchers at the Women's Global Health Imperative program at the University of California-San Francisco's Medical Center conducted a large-scale clinical trial with 5,045 women in Zimbabwe and South Africa to test the effectiveness of diaphragms in preventing the spread of HIV. However, the clinical trial found no statistical difference in the rate of new HIV infections in the two study arms: those who received a diaphragm plus lubricant along with male condoms for their partners, and those who only received male condoms.⁸¹

Candidate Vaginal Microbicide Concepts

Microbicides comprise a range of compounds that, applied topically prior to sexual intercourse, have the potential to prevent either partner from infection by HIV and a number of other STIs. Scientists have taken two general approaches to microbicide development: developing and testing new substances, and investigating the potential microbicidal activity of existing spermicidal products⁸². There are five basic mechanisms of action by which various candidate microbicides may work to prevent HIV and STDs.^{83,84, 85}

1. *Killing or inactivating infectious pathogens.* Some microbicides work by breaking down the surface or envelope of the virus or pathogen. Examples include surfactants (detergent-like chemicals) that disrupt the lipid membranes of cells and the lipid envelopes (surfaces) of viruses such as HIV and herpes, and certain antibiotics that increase membrane porosity. The surfactants include the existing spermicides *nonoxynol-9*, *octoxynol-9*, *benzalkonium chloride*, *menfegol*, and novel substances like *Savvy™*

⁷⁹ AIDS Vaccine Advocacy Coalition. Preventive HIV Vaccine Clinical Trials Around the World.

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

⁸⁰ AIDS Vaccine Clearinghouse. *Vaccine Science, Research & Product Development.*

<<http://aidsvaccineclearinghouse.org/science.htm>>

⁸¹ Padian, van der Straten, Ramjee, Chipato, de Bruyn, Blanchard, Shiboski, Montgomery, Fancher, Cheng, Rosenblum, van der Laan, Jewell, McIntyre; the MIRA Team. *Diaphragm and lubricant gel for prevention of HIV acquisition in southern African women: a randomized controlled trial.* *Lancet* 2007; 370: 251–61

⁸² The Case for Microbicides: A Global Priority WHO Fact Sheet No 242 *Women and HIV/AIDS*, June 2000.

<<http://www.who.int>>

⁸³ Interagency Coalition on AIDS and Development (2004). HIV/AIDS and Prevention Options for Women Fact Sheet. <http://www.icad-cisd.com/content/pub_details.cfm?id=23&CAT=9&lang=e>

⁸⁴ Global Campaign for Microbicides (May 2005). Fact Sheet #3: Microbicide Research and Development – What's in the Pipeline? < <http://www.global-campaign.org/clientfiles/FS3-Pipeline-May05.pdf>>

⁸⁵ Matthews, J and Harrison, T. (2006). An update on female-controlled methods for HIV prevention: Female condom, microbicides and cervical barriers. *The Southern African Journal of HIV Medicine*: Dec 2006.

that work in a similar way. For safety reasons, researchers have focused on surface-acting microbicidal agents that do not harm epithelium, the thin, protective layer of cells lining the vagina and rectum. *Nonoxynol-9* has already been tested and proven not to be an effective microbicide, and is potentially harmful.

Two clinical trials to examine the safety and effectiveness of *Savvy*TM as a potential microbicide for the prevention HIV transmission, conducted by Family Health International (FHI) and partners in Ghana and Nigeria, provided no evidence that *Savvy*TM prevents HIV infection. As of September, 2007, the results have not yet been published but a statement by FHI indicates that the Ghana trial (stopped in November 2005) suggested no difference in HIV risk among those who used *Savvy* and those who used a placebo. The second trial in Nigeria, halted in August 2006, suggested the possibility of increased risk with the use of *Savvy*TM, but it is possible that the result could have occurred by chance.⁸⁶

2. *Strengthening the body's normal defenses.* The vagina is normally too acidic for sperm to survive. During sexual intercourse semen, which is alkaline, neutralizes the acidity of the vagina, making it more likely that sperm — and also HIV and other pathogens — will survive. Acid-buffering microbicides make the semen acidic, thus keeping the vagina acidic and inactivating sperm and several STI organisms, including HIV. The body has several naturally occurring defense mechanisms that a microbicide may be able to supplement or enhance. *Lactobacillus*, for example, is naturally occurring, “good” bacteria that helps protect the vagina by maintaining its acidic environment. This natural acidity helps foster an inhospitable environment for many pathogens, including HIV. This approach seeks to enhance the vagina's naturally acidic environment and production of hydrogen peroxide, both of which are hostile to pathogens including HIV. Thus, the idea of developing a microbicide that supports the lactobacilli in performing this function is one potential mechanism of action being explored. Examples include *BufferGel*TM, *Acidform*TM gel, *Mucocept*TM, which help the vagina to maintain natural levels of acidity in the presence of semen, and suppositories containing *Lactobacillus*, which lives normally in the healthy vagina and which produces hydrogen peroxide.

3. *Creating physical barriers.* Gels or creams could provide a physical barrier between pathogens and vulnerable cells in the epithelium of the vagina or rectum. One example is the *Invisible Condom* which uses a water-soluble liquid polymer that turns into gel following application and contact with body heat, creating a barrier that could block HIV and other STIs.

⁸⁶ News Alert. 18 September 2007. *FHI Letter Regarding Further Analysis of Savvy Results*. <<http://www.global-campaign.org/clientfiles/FHI-Savvy-Statement.pdf>>

The Invisible Condom™ - Université Laval, Québec, Dr. Michel G. Bergeron and his team

The Invisible Condom,™ which is being developed by the Infectious Diseases Research Centre at Université Laval, is a microbicidal gel formulation designed to prevent the sexual transmission of HIV/AIDS and other STIs, as well as unwanted pregnancies and, possibly, cervical cancer. The gel offers both a physical barrier (by blocking pathogens and spermatozooids) and a chemical barrier (by destroying pathogens and spermatozooids). The gel is inserted into the vagina through a special vaginal applicator. The applicator is unique in that: it achieves uniform distribution of the gel; the gel is delivered efficiently and rapidly; the applicator is easy to manipulate and insert; the applicator polymer is compatible with the gel; and there is no leakage.

Work done in laboratory and on animals has shown that the gel formulation can prevent HIV and other STIs such as Chlamydia and gonorrhoea and HSV-2. Four phase I trials have been completed. The trials revealed that:

- there was no change in the presence of lactobacillus in the vagina, which is necessary to maintain a healthy vagina;
- there was no change in the normal vaginal pH;
- the gel was well distributed in the whole vagina, the cervix and the posterior fornix;
- the gel stayed in the vagina for 4-8 hours after its application; and
- the gel was safe and highly acceptable to women.

Other factors that make the Invisible Condom™ unique are that it is tasteless and odourless, that its presence is imperceptible, and that there is no vaginal leakage. A phase I/II trial in Cameroon (with CIHR funding) was recently completed. The trial data and safety monitoring board (DSMB) reviewed and approved the safety data of phase I part of the trial in 252 women and allowed phase II part to start immediately after. Presently, phase II results (200 women) are being analyzed. Next is a multi-site phase II/III trial of the Invisible Condom™ that is being planned in nearly 5000 women at high-risk of acquiring HIV and that can begin in 2008 as soon as funds are available.

4. Inhibiting viral entry. In order for HIV to infect a cell, particular viral proteins must bind themselves to matching receptors on the target cell's membrane. Some candidate microbicides seek to interrupt this process by introducing other molecules that will bind with the receptors in advance, thus blocking the sites and preventing HIV attachment. Some of these products are nonspecific blockers, which means that they act against multiple organisms, including microbes that cause HIV and other STIs. In some cases, the products work by attaching themselves to pathogens, thus preventing them from attaching to host cells. Other products bind to potential host target cells, forming a protective coating that prevents pathogens from attaching. Examples include sulphated and sulphonated polymers such as *Carraguard™*, *PRO 2000*, *Ushercell™*, and *Emmelle*.

Ushercell™ (cellulose sulphate) - Polydex Pharmaceuticals Limited, Toronto

Ushercell (cellulose sulphate) is a natural, cotton-based gel compound that acts as a barrier to HIV, sperm and other STIs. Ushercell has shown promising broad-spectrum prevention capabilities with a strong safety profile. In vitro results indicate Ushercell's potential to prevent the spread of Herpes 1 and 2, chlamydia trachomatis, gonorrhoea, human papilloma virus, and HIV. Ushercell has also shown encouraging results in trials that studied Bacterial Vaginosis, a common vaginal disorder and known HIV risk contributor, and is currently engaged in a Phase II clinical trial in Brazil to determine efficacy for treatment and prevention of BV, results of which should be available in late 2006.

Ushercell has demonstrated 96% effectiveness at preventing pregnancy, when used as directed, in recent contraceptive clinical trials conducted in the United States.

Ushercell is owned, developed and a patented product of Polydex Pharmaceuticals Limited, a small Toronto-based pharmaceutical developer and producer. Polydex is committed to the development of Ushercell and to the provision of a viable HIV prevention microbicide at humanitarian price levels to collaborative organizations, aiming to make a world of difference for people in developing countries where prevention strategies are needed now.

In January of 2007, Phase III trials were stopped over concerns surrounding the rate of seroconversions. The Data Safety and Monitoring Boards (DSMB) of CONRAD met and based on a review of preliminary data, recommended that the Phase III trial of the candidate microbicide Cellulose Sulfate (CS) in Benin, India, Uganda and South Africa be discontinued. Data indicate that CS may have contributed to an increased risk of HIV infection among participants who used the product, compared to participants who received the placebo. Presently, scientists are struggling to determine the cause, given that 11 earlier safety trials had not revealed any safety concerns.

Source: <www.thelancet.com> Vol 369, March 3, 2007

5. *Inhibiting viral replication.* Some candidate microbicides are being developed from the anti-retroviral drugs that HIV positive people use to lower the amount of virus in their bodies. Formulated as gels or creams, these drugs may be able to suppress replication of any HIV that enters the vagina or rectum during sex. If so, they could substantially lower the odds that the microbicide user will become infected. Examples include antiretroviral agents like *PMPA gel*, which prevents HIV from replicating in cells, and *plantibodies*, anti-HIV antibodies genetically engineered from plants that would combat pathogens before infection occurs. Many replication inhibitors were initially explored as potential HIV therapies but were found to be inadequate for that purpose because they are not absorbed easily into the bloodstream. However, some of these same compounds are now being evaluated as potential microbicides because they can be applied topically and not absorbed systemically. Concepts in development include tenofovir, TMC-120, MC-1220, UC-781, and MIV-150.

International Partnership for Microbicides

The International Partnership for Microbicides (IPM) is a non-profit product development partnership (PDP) founded in 2002. IPM's goal is to reduce HIV transmission by accelerating the development of and accessibility to safe and effective microbicides for women in developing countries. Through its partnerships with private sector (pharma, biotechnology and clinical research organizations), as well as non-profit and academic organizations, IPM is working to increase the efficiency of microbicide product development and testing.

Under IPM, a variety of microbicide research and development activities are, or will be, taking place. These include: screening compounds, designing optimal formulations, in-licensing and development of microbicide drugs, establishing manufacturing capacity for safety trials, developing clinical trial sites, conducting safety trials and conducting a large-scale efficacy trial. IPM identifies the most promising technologies and invests its resources to help develop them into usable products.

IPM is concentrating on antiretrovirals (ARVs) as the backbone of next- or second-generation products. IPM is supporting or developing many of these products, leading this effort with dapivirine (TMC 120 gel), a non-nucleotide reverse transcriptase inhibitor (NNRTI) licensed from Tibotec Pharmaceuticals, Ltd. (a subsidiary of Johnson & Johnson). Dapivirine is currently in advanced safety studies.

IPM is also developing two entry inhibitors, one licensed from Merck & Co, Inc. and the other licensed from Bristol-Myers Squibb. One of these drugs attaches to the virus itself, rendering it unable to properly attach to the cell, and the other attaches to a receptor on the cell, also interfering with viral/cell interactions. Both of these compounds are in the pre-clinical stage and IPM is working as quickly as possible to advance them to clinical trials. IPM anticipates these two drugs will be used together and/or in combination with other ARVs.

Ideally, a microbicide would combine more than one of the five mechanisms described above for extra effectiveness. Products currently being tested have a number of attractive features⁸⁷:

- Some products being investigated prevent pregnancy; others do not.
- Many candidate products are widely anti-microbial and could provide protection against a range of STIs.
- Microbicides would help protect both insertive and receptive sexual partners.
- Some microbicides are likely to be available over the counter, so they can be distributed like condoms in stores, kiosks or through peer promoters.
- Many candidate products are likely to be inexpensive.

More than 15 candidate microbicides are currently being studied in clinical trials. Their mechanisms of action include disruption of the viral membrane by surfactants, maintenance of an acidic vaginal pH, binding to the viral envelope to block receptor binding, and blocking of receptors; they may also be combined with antiretroviral drugs⁸⁸. The development of safe and effective microbicides has been delayed by limitations in understanding the biological processes of HIV transmission, difficulties in extrapolation from animal models, lack of established correlates of protection, and the need to enroll and follow large cohorts of high-risk participants for several years in order to demonstrate efficacy. The table below provides an overview of microbicides in clinical (human) trials as of November 2007.

⁸⁷ Report of the 2nd Canadian Microbicides Symposium. <http://www.acpd.ca/pdf/micro_sym_report_en.pdf>

⁸⁸ Darpun Dhawan¹ and Kenneth H. Mayer. *Microbicides to Prevent HIV Transmission: Overcoming Obstacles to Chemical Barrier Protection*. JID 2006:193 (1 January)

Microbicide Candidates in Ongoing Clinical Trials: Summary as of November 2007			
Source : 2007 Alliance for Microbicide Development			
Phase	Candidate Name and Formulation	Mechanism of Action	Sites by Country
3	Carraguard® gel†	Entry/fusion inhibitor	South Africa
	0.5% and 2% PRO 2000/5 gels	Entry/fusion inhibitor	South Africa, Tanzania, Uganda, Zambia
2B	1% Tenofovir gel (“CAPRISA 004”)	Replication inhibitor	South Africa
2/2B	0.5% PRO 2000/5 gel (P) and BufferGel® (“HPTN 035”)	Entry/fusion inhibitor and Vaginal defense enhancer	Malawi, South Africa, United States, Zambia, Zimbabwe
2	1% Tenofovir/PMPA gel	Replication inhibitor	India, United States
1/2	Dapivirine (TMC120) vaginal ring†	Replication inhibitor	Belgium
	Dapivirine (TMC120) gel†	Replication inhibitor	Rwanda, South Africa, Tanzania
	Invisible Condom™ gel	Entry/fusion inhibitor	Cameroon
1	Dapivirine (TMC120) vaginal ring	Replication inhibitor	Belgium
	Dapivirine (TMC120) gel†	Replication inhibitor	South Africa
	1% Tenofovir/PMPA gel	Replication inhibitor	Dominican Republic, United States
	0.1% UC-781 gel	Replication inhibitor	United States
	0.1% and 0.25% UC-781 gel	Replication inhibitor	United States
	0.1% and 0.25% UC-781 gel	Replication inhibitor	Thailand
	3% VivaGel™ (SPL7013 gel)	Entry/fusion inhibitor	Puerto Rico, United States
	3% VivaGel™ (SPL7013 gel)	Entry/fusion inhibitor	Kenya, United States
N/A	Vaginal ring safety and acceptability study	Placebo ring±	Kenya, South Africa, Tanzania

*AMD is in the process of modifying its reports on clinical trials of microbicides in all relevant formulations.
†These trials have completed and analysis of the final results is ongoing
± This device is intended for use with a microbicide.

Candidate Rectal Microbicides Concepts⁸⁹

Discussion of topical microbicides so far has mostly focused on vaginal use for a number of reasons. As noted above, women are more vulnerable to HIV transmission because of their genital ecology and because many of them have limited or no control over safe sex decisions. The science of developing a rectal microbicide presents its own set of challenges as well. Few resources have been allocated to address these challenges so far. Heterosexism has inhibited a broader discussion of anal sex practices and rectal microbicides. There is a general lack of recognition that heterosexual contacts also include anal intercourse, and that efforts by young women to protect their virginity or prevent pregnancy increasingly translates into more anal sex. The silence shrouding the issue of anal sex among heterosexuals and of gay male sexuality in general is one of the barriers to better HIV

⁸⁹ By Betsy M. Finley and Carolyn J. Plescia (Winter 2005/2006). The Future of HIV Prevention: New Tools, New Hope. <<http://www.thebody.com/content/treat/art14134.html>>

prevention and microbicides development. It was noted by some consultation informants that Canada has an important leadership role to play in advancing rectal microbicides research, development and advocacy.

Canada has traditionally been better able to discuss sex and drugs in ways other than punitive and shaming. It's very challenging in the US, so we're always looking to our friends outside our borders who are more able to talk about anal sex. We are hoping that Canada and European partners are able to advance rectal microbicides work. (Interview #29)

Over two dozen potential microbicides are being investigated for possible vaginal use but it is not clear yet whether any of them will be suitable for rectal use. The rectum and the vagina have very different structures and natural ecologies. The vagina, for example, is a closed pouch while the rectum is part of an open-ended cavity. A greater quantity of the microbicide product is likely to be required for adequate rectal coverage than for effective vaginal use. The development of rectal microbicides is at a much earlier stage than vaginal microbicides, partly because the environments of the rectum and vagina are markedly different. Early research is being conducted to find markers that could be used to study the safety of rectal microbicides. Studies are also being done to determine the acceptability, when used rectally, of different volumes of a gel that is similar to potential microbicides. Given the differences in the tissues and structures of the vagina and rectum, more research is needed to assess the potential of microbicides for rectal use.

More immune cells with CD4 receptors and more CD4 receptors per cell make rectal mucosa particularly vulnerable to HIV infection. The rectal lining is more fragile than most of the tissue lining the vagina. These factors further enhance rectal vulnerability to irritation, tearing and infection during sex. Clinical trials are beginning to fill a huge gap in knowledge about how rectal sex affects the lining of the rectum. This information will help scientists identify products that could offer additional protection. It will also establish a baseline for evaluating whether a candidate product increases rectal vulnerability to HIV infection.

"Male Tolerance" trials are studying whether potential microbicides cause irritation on the penis or within the male urethra. This information is vital to the successful introduction of both vaginal and rectal microbicides, since a product that increases risk of exposure or is irritating to the insertive partner would be unacceptable. The safety and acceptability of penile application of two potential microbicides (BufferGel and PRO 2000 Gel) were recently assessed in healthy low-risk men and HIV-positive men; no serious adverse events or urethral inflammation were detected.⁹⁰ PRO 2000 is poised for clinical trials in the near future.

A non-nucleoside reverse transcriptase inhibitor, UC-781, is currently undergoing phase I clinical trials as a rectal microbicide. This study tests the safety and applicability of UC-781 for rectal use, using the vaginal microbicide gel formulation. UCLA is also planning pre-clinical and formulation work for a rectal-specific microbicide with the aim of starting another Phase I trial as well.

⁹⁰ SR. Tabet, MM. Callahan, CF. Mauck, F. Gai, AS. Coletti, AT. Profi, et al, "Safety and Acceptability of Penile Application of 2 Candidate Topical Microbicides: BufferGel and PROGEL: 3 Randomized Trials in Health Low-Risk Men and HIV-Positive Men," *Journal of Acquired Immune Deficiency Syndrome*, 33(4), August 2003: 476-483.

Canada's Commitments

Canada Can Make a Difference

Canada can make a difference in the global effort to develop microbicides. Canada should pursue a continuum of activities as a coordinated effort, partnering with other countries and integrating lessons learned globally into the Canadian experience, and ensuring that expertise developed in other countries is applied in Canada. Furthermore, Canada is one of the few countries that have the ability to work proficiently in both Anglophone and Francophone environments.

Effective International Collaboration

Canadian researchers also have over 20 years of experience and strong working relationships in developing countries in Africa and other parts of the world. Many of these researchers have demonstrated commitment to working internationally, and are willing to continue contributing. More specifically, Canada has contributed to capacity building for developing countries with respect to clinical trials and has developed the Global Health Research Initiative⁹¹ which aims to shape and respond to the global health research agenda, influence policy and policy coherence relating to global health research and, facilitate information sharing among partner agencies. The Canadian government has already demonstrated its leadership and commitment to developing new prevention technologies for HIV/AIDS by providing funding for international vaccine and microbicide initiatives. Support for international research efforts must continue and support for domestic research efforts must be enhanced.

At the global level, the Canadian International Development Agency (CIDA) is a major contributor to HIV/AIDS efforts. Since 2001, CIDA's five-year cumulative investment in the global response to HIV/AIDS is over \$800 million. CIDA has contributed over \$750 million towards efforts to address HIV/AIDS in developing countries and has recently made a number of significant new commitments, including supporting the Canadian HIV Vaccine Initiative, \$250 million over the past two years to the Global Fund to fight AIDS, TB and Malaria, and \$120 million announced on World AIDS Day 2006 in support of various initiatives through Canadian, international and developing country partners. With regards to microbicides, the Canadian government committed a total of \$30 million over five years to the IPM, gave \$350,000 in collaboration with Health Canada to Université Laval (for Dr. Michel G. Bergeron's *Invisible Condom*[®]), and has sponsored microbicides Symposia and the 2006 Microbicides Conference in Cape Town. The CIHR has also funded Phase I/II clinical trial of the *Invisible Condom*[®] with 452 healthy women in Cameroon.

The Department of Foreign Affairs and International Trade (DFAIT) is also taking an increasingly active role in addressing the international dimensions of HIV/AIDS. Other departments and agencies that have invested resources in HIV/AIDS include PHAC and Health Canada, Citizenship and Immigration Canada, Justice Canada, and Human Resources and Social Development Canada.

⁹¹ The Global Health Research Initiative is an agreement of cooperation between the Canadian Institutes of Health Research, Canadian International Development Agency, Health Canada, and the International Development Research Centre aimed at coordinating and building upon Canada's global health research activities. <<http://www.cihr-irsc.gc.ca/e/7350.html>>

United Nations Special Session on HIV/AIDS – Declaration of Commitment⁹²

As part of the UNGASS Declaration of Commitment on HIV/AIDS, Canada agreed to “increase and accelerate research on HIV vaccines and increase research to improve prevention, care, treatment, women-controlled methods of prevention, microbicides and the means to prevent mother-to-child transmission.”

Leading Together: Canada Takes Action on HIV/AIDS (2005-2010)⁹³

Canada’s multi-stakeholder plan, *Leading Together: Canada Takes Action on HIV/AIDS (2005-2010)*, commits to Canadian contributions of research and expertise by “participating in global research efforts to develop HIV/AIDS treatments, technologies, vaccines, microbicides and prevention strategies and to identify effective ways to provide care within existing health systems.”

The Federal Initiative to Address HIV/AIDS in Canada⁹⁴

In May 2004, the Government of Canada announced that funding for the *Federal Initiative* would increase from \$42.2 million in 2003-2004 to \$84.4 million annually by 2008-2009. The *Federal Initiative to Address HIV/AIDS in Canada* identifies five areas for increased federal action and investment: program and policy interventions; knowledge development; communications and social marketing; coordination, planning, evaluation and reporting; and global engagement. Activities will be undertaken in partnership with community organizations, other federal government departments and agencies and other levels of government.

The *Federal Initiative* aims to develop discrete approaches to addressing the epidemic for vulnerable groups such as “women at risk for HIV infection.” The *Federal Initiative’s* “Knowledge Development” area of action states that: “Programs will be developed to enhance research on new prevention technologies, such as vaccines and microbicides.” Under the “Global Engagement” area of action, the *Federal Initiative* commits that: “In collaboration with CIDA, Foreign Affairs Canada and others, technical support and policy guidance will be provided on global issues, such as gender risk factors, human rights, microbicides, vaccines and harm reduction.”

Canada’s International Policy Statement⁹⁵

The International Policy Statement sets out the Government’s international direction and priorities in diplomacy, defense, international commerce and development. The International Policy Statement specifies under “Building Genuine Development” that one area of priority for the Government of Canada is the Millennium Development Goals (MDGs) on governance, private sector development, health, basic education and environmental sustainability, and ensuring our development assistance efforts systematically incorporate gender equality throughout. HIV/AIDS was specified as one of the key initiatives under this area of priority.

The health and education sectors rank high in all the priority requests to Canada for assistance from developing countries. In health, two major strengths explain this demand. Canada’s longstanding experience in strengthening accessible health care systems at home and abroad has been reinforced by its clear global leadership in recent years in fighting communicable diseases; strengthening sexual

⁹² <http://www.ungasshiv.org/index.php/ungass/ungass/declaration_of_commitment>

⁹³ *Leading Together: Canada Takes Action on HIV/AIDS (2005 - 2010)*. <<http://www.leadingtogether.ca/index.html>>

⁹⁴ *The Federal Initiative to Address HIV/AIDS in Canada Strengthening Federal Action in the Canadian Response to HIV/AIDS*. <<http://www.phac-aspc.gc.ca/aids-sida/fi-if/fa-if/index.html>>

⁹⁵ *Canada’s International Policy Statement - A Role of Pride and Influence in the World*. <<http://www.itcan-cican.gc.ca/ips/menu-en.asp>>

and reproductive health (especially for women); and improving infant and child health and food security.

Rationale

Potential Impact of Microbicides

While microbicides will have the greatest impact in the developing world in countries most affected by HIV and other STIs, there is also an important potential role for microbicides in reducing HIV and STIs in developed countries. As noted earlier, women represent nearly a quarter of new HIV infections in Canada. In addition, there is a potentially large and lucrative market for microbicides among men who have sex with men and among women at risk of other STIs, such as chlamydia⁹⁶.

Canada can Take a Leadership Role

On World AIDS Day 2004, the Government of Canada announced significant investments towards microbicides and other initiatives to prevent infections among women and youth. Canada could show further leadership by becoming the first country in the world to develop a microbicide plan. Participants of the 2005 Canadian Microbicides Symposium called for the development of this CMAP, which would outline Canada's contributions to microbicide development, delivery and equitable access both domestically and internationally. It would be linked to the Canadian HIV Vaccines Plan currently under development.⁹⁷

We're very much looking forward to this Action Plan. It's an important step for North America and the world. There is no other country that has a microbicides action plan, somebody has to be the first. This will enable us to provide a model to other countries that will pave the way for concerted efforts. (Interview #31)

Some of the ways in which Canada was seen by consultation informants to be able to contribute to the global microbicides research and development effort include:

- continue acting as a donor for global microbicides efforts
- conduct trials in developing country settings
- continue advocacy efforts in international policy discussions (e.g., G8, UNGASS, MDGs)
- lead in building microbicides preparedness strategies
- lead in ensuring distribution and post-market surveillance of microbicides globally
- monitor and evaluate microbicides distribution and access
- initiate an international regulatory body to facilitate access and distribution
- act as a counter-balance to other countries' abstinence-based policies and influence on the global agenda on sexual and reproductive health and rights
- lead in advancing rectal microbicides research, awareness and advocacy
- build on Canada's strong gender- and human rights-based policy positions to promote microbicides

⁹⁶ The Case for Microbicides: A Global Priority WHO Fact Sheet No 242 *Women and HIV/AIDS*, June 2000. <<http://www.who.int>>

⁹⁷ Microbicides Position Statement, Canadian AIDS Society, October 2004.

One big advantage is Canada's sane approach to sexuality and HIV prevention relative to the US. Canadians are a little more comfortable with the fact that people are sexually active. The precedent that Canada sets in placing microbicides along the continuum of prevention will be very important...and taking into account how different populations need to be engaged in unique ways. (Interview #31)

I would like to see Canada stay at the cutting edge in terms of sexual and drug-related harm reduction. Microbicides will be harm reduction, as with any preventive device. It fits well with the work that Canada does in harm reduction, fits with the language that we've developed to support harm reduction rather than the focus on abstinence. Canada seems more able to accept some basic human behaviours, such as using substances, it's so much more humane. That ideology of meeting human beings where they are to make the best decisions that they can make - will be very relevant to microbicides. (Interview #29)

The Need for Collaboration

Despite the urgent need for microbicides and their scientific and public health promise, microbicides are a classic example of a product that will not reach the market without public-sector support. It is clear that the private sector alone will not take forward microbicide research and development and that the current level of public investment, while growing, is insufficient to accelerate and support the full process of bringing a product to market.

Given the limited availability of financial resources and limited number of clinical trial sites, it is critical that product development and testing be conducted efficiently to produce one or more products that are safe, effective, and available. The major stakeholders in microbicide research and development, including donors, industry and scientists, need to collaborate to develop a scientific strategic plan and an agreed-upon set of criteria for determining which candidate products should be given priority for advancement. Building on this strategy and on existing initiatives, an appropriate mechanism and scientific review process are needed to raise and allocate greatly increased funding to specifically target bottlenecks in the R&D process. For some public-sector and foundation donors, this will be critical to attracting or increasing their investment.⁹⁸

⁹⁸ The Case for Microbicides: A Global Priority WHO Fact Sheet No 242 *Women and HIV/AIDS*, June 2000.
<<http://www.who.int>>

Multi-Sectoral Stakeholder Engagement

CMAP as a Model of Multi-Sectoral Collaboration

Multi-sectoral collaboration is essential for the development of a meaningful Action Plan to support the development and eventual introduction of microbicides in Canada and around the world. During three successful Symposia on Microbicides held in Canada in October 2003, March 2005 and April 2006, representatives from various sectors (government, industry, community, research) jointly identified the need for a multi-sectoral microbicides Action Plan to articulate domestic and global contributions from Canada. A Steering Committee made up of representatives from these sectors undertook to develop the CMAP, which positions microbicides strategically within broader Canadian HIV/AIDS strategies and in relation to the Canadian HIV Vaccines Plan.

To develop the CMAP, the steering committee conducted an environmental scan to identify Canadian involvement and expertise in microbicides research and development, and identified areas in which Canadian expertise can best be applied to meet global and Canadian needs in the field. The CMAP includes recommendations on policy and regulatory issues, cross-departmental and cross-sector mechanisms for collaboration, and identifies steps to strengthen commitments to accelerate microbicides development and delivery.

Canada is the first country in the world to develop a multi-sector microbicides Action Plan outlining domestic and global contributions, and could serve as a model in the field.

To ensure the success of a long-term initiative such as a microbicides Action Plan, it is necessary to enhance collaborative working relationships between government, civil society and private sector, and to ensure decision-making and direction setting processes are consistent, shared and open. There must also be collaboration across the scientific fields of basic science (discovery of new compounds and microbicide candidates), clinical science (testing candidate products through clinical trials), epidemiology (studying viral transmission in populations), and social sciences (studying preparedness and acceptance issues).

A multi-sectoral Steering Committee has called for the development of a Canadian microbicides plan which would outline Canada's contribution domestically and internationally from multiple sectors (government, research, community, and private)⁹⁹. The Symposium participants discussed the various ways in which Canada could show leadership:

- advocacy
- twinning between NGOs
- basic, clinical, socio-behavioural, and community-based research
- supportive programming and policy
- resource mobilization

Each of these areas is elaborated in various sections that follow, based on document review and consultation interviews with key stakeholders from all of the relevant sectors.

⁹⁹ Report of the 2nd Canadian Microbicides Symposium. <http://www.acpd.ca/pdf/micro_sym_report_en.pdf>

MAG-Net

The Microbicide Advocacy Group Network (MAG-Net) is a coalition of 60 Canadian AIDS service organizations, sexual and reproductive health organizations, international development NGOs and advocates interested in promoting the development of alternative HIV/AIDS and STI prevention options, particularly microbicides. MAG-Net is coordinated by the Canadian AIDS Society (CAS) and serves as the Canadian partner of the Global Campaign for Microbicides (GCM), an international coalition of more than 200 NGOs worldwide that collaborate on access and advocacy issues. MAG-Net members, coordinated by the Canadian AIDS Society, have been advocating for a significant Canadian contribution to microbicides development for over four years. MAG-Net aims to share ideas and resources on raising awareness of microbicides with other CAS members and partners, and share ideas and provide input into coordinated advocacy efforts at local, national and global levels.

Sector Roles in Microbicides

The following table summarizes the sector-specific roles identified by stakeholders in helping Canada make progress towards microbicides research and development. All stakeholders, across all sectors, felt that it was their responsibility to remain updated on new developments in microbicides research, contribute to advocacy efforts to support microbicides research efforts, and to promote microbicides within their own constituencies. Many organizations not directly involved in microbicides research have joined MAG-Net and have developed position statements endorsing microbicides.

Sector	Roles
Community-Based HIV/AIDS Organizations, Women's Sexual and Reproductive Health Organizations, and International Development NGOs	<ul style="list-style-type: none"> ○ endorse and advocate for microbicides research ○ develop community competence and preparedness for microbicides ○ raise awareness about the role community based organizations can play before, during and after trials ○ link with local communities and resources to facilitate clinical trial recruitment ○ bring microbicides into education and training programs in communities, like with ARVs and PMTCT programs, working with reproductive age groups of women and men, and also among sex trade workers ○ participate in advocacy, public education and awareness raising amongst partners and local communities ○ incorporate microbicides education in international sexual and reproductive health projects ○ assist in understanding acceptance and distribution issues and develop strategies for facilitating microbicides use by women ○ provide leadership in negotiating delivery and access through the regulatory systems. Advocate when manufacturers are making the application for licensing ○ provide education, presentations, communications, to members and clients, customizing information for specific vulnerable populations ○ lead advocacy initiatives to promote investment in, and awareness of, microbicides

Sector	Roles
Basic Science Researchers	<ul style="list-style-type: none"> ○ lead the scientific discovery and development of microbicide candidate concepts and products ○ ensure that an adequate pipeline of new concepts flow through Canadian research institutions, new researchers are trained in microbicides science, and advocate for adequate funding
Clinical Researchers	<ul style="list-style-type: none"> ○ lead the clinical testing of candidate microbicide products, testing efficacy as well as issues of acceptance and accessibility ○ establish and maintain the highest standards of ethical conduct of clinical trials
Social Researchers	<ul style="list-style-type: none"> ○ conduct research on acceptability, preparedness, access and delivery issues ○ work alongside clinical research to understand usability and acceptance of microbicides
Government	<ul style="list-style-type: none"> ○ provide funding for Microbicides Symposia, IPM, microbicides research through open and strategic CIHR programs, research conferences ○ coordinate domestic and global efforts ○ promote domestic and international policy that supports microbicide development and delivery ○ ensure microbicides are included in discussions and resolutions on UN commissions, WHO, APEC, G8, UNGASS
Industry	<ul style="list-style-type: none"> ○ invest in research and development, manufacturing and production ○ be willing to share intellectual property in order to accelerate microbicides development
Public Health Sector	<ul style="list-style-type: none"> ○ monitoring, prevention and control of HIV/AIDS and STIs ○ help with microbicides delivery, education and access ○ translate lessons learned from delivery of other contraceptive or prevention technologies

COMPONENTS OF THE CANADIAN MICROBICIDES ACTION PLAN

1. Funding

Microbicides have an important place in the broader effort to reduce the spread of HIV/AIDS, both in Canada and globally. The development of an effective microbicide would offer new options for women and men to protect themselves against HIV infection. It would make ongoing prevention efforts easier for those who are already living with HIV and who fear infecting or re-infecting their partners. And it should be possible to find an effective microbicide in a much shorter time-frame than that projected for the development of vaccines. For all these reasons, Canada and other nations need to assess how they can best support microbicide research.

The Perspective of one Pharmaceutical Company ~ Polydex Pharmaceuticals Ltd.

Polydex is a very small company with annual sales in the range of \$7 million. We have been trying to develop a cellulose sulphate compound that may have anti-HIV activity and that may prevent conception and the transmission of STIs. The development process has proved somewhat challenging at times. Without the funding we get from several agencies and philanthropists, we would not have been able to come as far as we have.

The two most significant challenges facing the developer of a microbicide are funding and the consistent production of the compound. We have managed the production. Raising funds is another matter. It is estimated that it takes more than \$700 million and over ten years of unwavering research and development to come up with a new product. Large pharmaceutical companies seem to want phase III clinical data before they will consider investing.

Canada can help by making a greater contribution to microbicide research and development. But gaining the necessary funding and support would be a lot easier if there were a better understanding of the potential impact of effective microbicides on HIV and other diseases. Our development teams see the successful development of an effective microbicide as not just a moral imperative, but also a commercial opportunity. We regard many developing countries as important potential markets.

Source: Proceedings of the Microbicides Symposium, Ottawa, Ontario – 30 October 2003.

Funding Barriers

Virtually all microbicide research to date has been conducted by non-profit and academic institutions or small biotech companies and funded by charitable foundations and government grants. These public funds also support basic science, social and behavioral research, and clinical trial infrastructure that contribute to microbicide research and development. Large pharmaceutical companies have not invested significantly in this field, primarily because microbicides are a classic “public health good” which would yield tremendous benefits to society but for which the profit incentive to private investment is low.¹⁰⁰

Despite potential benefits of microbicides, pharmaceutical companies do not seem eager to invest in their development and research. Even if less than 10% of sexually active women in industrialized and developing countries use a basic microbicide, the market for microbicides by 2011 could be US

¹⁰⁰ Fact Sheet #2: Frequently Asked Questions About Microbicides. <[http://www.global-campaign.org/clientfiles/FS2-FAQs\[E\]07.pdf](http://www.global-campaign.org/clientfiles/FS2-FAQs[E]07.pdf)>

\$900 million, and potentially double that by 2020.¹⁰¹ Despite the potential size of the market, pharmaceutical companies have not made significant investments in the field.¹⁰² In part, this has happened for the following reasons:

Low Initial Return on Investment. To date, there has been little interest from the pharmaceutical industry, outside of biotech companies, in the development of microbicides, and the burden of funding has fallen on the public and charitable sectors. This reliance on non-private funding has led to the new agents being developed in the academic sector, which has probably slowed progress even though the approach has been highly cost effective¹⁰³. Many pharmaceutical companies are reluctant to invest because it would take a high initial investment, and future products will have to be sold inexpensively, which may make it difficult to quickly re-coup investments. In the case of the first generation of microbicides, it is unlikely that initial returns could cover development costs if the products are sold at affordable prices, particularly in low-income countries. Firms and organizations currently developing products are doing so with significant support from donors. However, depending on the market's evolution, a second generation product could be self-funding and a third generation product could bring significant returns.

Difficulties Around Research and Clinical Trials. Even though research for a new product is difficult, several issues relating to clinical trials impede donors' willingness to invest in microbicides research. Some of these issues are:

- Difficulties in obtaining informed consent. This remains one of the major challenges in the conduct of vaginal microbicide effectiveness trials in the developing world.
- Dealing with suspicion and HIV/AIDS related stigma.
- Ensuring sustained use of known prevention methods, such as condoms and quality HIV prevention education and counseling.
- Ethical concerns about seroconversion during the study and related to this, access to treatment in countries where there is limited access to anti-retroviral treatments.
- Difficulties with maintaining confidentiality of HIV results at screening.
- Concerns around compensation/incentives for participation in clinical trials
- Ongoing provision of standard of care for people who become HIV-positive during clinical trials

Liability. Some pharmaceutical and biotech companies may be concerned by the possibility that microbicide users may take legal action if the product were to fail to protect them from an STI. Given that product liability usually involves inadequate communication of the likelihood and degree of risk to the consumer, special attention should be paid to clear and understandable labeling, consumer education, and post-market surveillance.

Good labeling entails communication of an appropriate level of information about the product, as well as its risks and potential side-effects. To ensure effective labeling and consumer education, pharmaceutical and biotech companies should involve community representatives in the research and development process. Off-label use of microbicides will especially be of concern with products that are ARV-based (and the risks of ARV-resistance), and with respect to rectal use of microbicides designed for vaginal use.

One of the biggest problems with microbicides R&D is that pharmaceuticals are not interested in it. They are making a lot of money from selling HIV drugs, and they are about making money. We can't rely on pharmaceuticals, because they don't see much in it for them. They see it as focusing on developing countries. (Interview #16)

Unless rich governments put in the money for R&D, unless governments invest in it, we'll have a big gap in the funding required to bring products to market. Pharma will jump on board when they see a product reaching a viable compound for marketing. (Interviews #26)

Lack of Governmental Commitment. Due to the reluctance of pharmaceutical and biotech companies to invest heavily in the research and development of microbicides, the first generation microbicide will likely need significant financial support from government agencies. Thus far, governments have been slow in establishing a funding program to bring microbicides to market.

Markets and Profitability

Perceptions about potential markets and profitability are a significant barrier to private sector investment in microbicides. Industry has generally assumed that the profitability of microbicides would be limited because the primary market would be in developing countries, that women in these resource-poor settings would have limited willingness and ability to pay, and that there would be considerable pressure to distribute microbicides inexpensively. However, findings from the two major market studies conducted to date suggest that the developed country market could be substantial and that women in low-income countries would be willing to pay for microbicides.

An American survey concluded that there are potentially 7.7 million women in the US who would be “very interested” in a microbicide at a cost roughly twice that of a male condom. Even if the product were not 100% effective, the number of women “very interested” would still be around 4 million. In a European market study, 25% of urban women surveyed in France thought a microbicide would be “very useful.” The European study also showed that women in developing countries would be prepared to pay a relatively high price to protect themselves from infection, especially when they think they are at high risk of acquiring HIV and other STIs. More than 60% of women surveyed in Ivory Coast and Kenya expressed willingness to pay up to five times the price of a male condom. The potential value of the market in urban Kenya for a microbicide that costs twice the price of a condom was estimated at \$3.8 million a year. In Brazil, potential annual sales could be worth \$800 million.¹⁰⁴

Industry is not engaged in microbicides research because they think that they won't make money - but they forget that it's not just poor people that have sex. If a company took a strong microbicide product, they'd make a fortune. I'm convinced of that. There's a lot of money to be made in the business of microbicides. Right now we're focused everything towards the market in Africa and developing countries, but we should focus on both developed and developing country markets. (Interview #20)

The Need for Public Investment in Microbicide Research¹⁰⁵

Before they can have a payoff in terms of prevention, microbicides must go through a long and expensive research and development process. Unfortunately, as with other important prevention technologies such as vaccines, large pharmaceutical companies are not interested in microbicide research and development. They cite concerns about liability and an uncertain regulatory environment, as well as the perceived lack of a sufficient market to make their investment profitable.

Microbicides aren't the only products to be ignored by pharmaceuticals. There are several products, such as malaria vaccines and new contraceptives, which would also yield huge returns to society in terms of productivity and health benefits, but hold little profit potential for private investors. Such products are known as ‘public health goods’ and they are developed only if government and foundations invest the necessary funds.

¹⁰⁴ The Case for Microbicides: A Global Priority. Second Edition, 2001.

<<http://www.microbicide.org/microbicideinfo/reference/case.for.microbicides.2001.pdf>>

¹⁰⁵ Canadian AIDS Society (2005). Microbicides Community Mobilization Kit.

<<http://www.cdn aids.ca/web/repguide.nsf/pages/cas-rep-0006>>

Several small biotechnology companies and university researchers are actively engaged in microbicide research but they rely entirely on government grants and contributions from foundations. Unfortunately, at the current levels, these funds are not sufficient. There is a backlog in the research and development pipeline, so that innovative and promising product concepts are languishing, while HIV infection rates are growing.

Given the expense of clinical trials and the scarcity of resources available, money has become the limiting factor in how rapidly microbicide research can proceed. Thus, advocacy efforts must focus on securing stable and adequate resources to ensure a microbicide is available by the end of this decade. The public sector will likely have to take the lead in microbicide research and development.

The cost of producing products

Development of experimental microbicides involves both a formulation (e.g., a gel, cream, or foam), a delivery device (e.g., applicator or vaginal ring), and product packaging. To have their candidate microbicide product considered for clinical evaluation, product sponsors must demonstrate that it has a consistent and stable formulation with ample laboratory and animal safety data. These candidate products then have to be produced in large quantities for clinical trials, an expensive step that must be taken long before it is known whether they are effective. For example, a Phase 1 trial involving 30 volunteers can require 1,000 applicators and individual product doses — a challenge for small biotech companies or university teams to produce.

Over the next five years, more than a dozen microbicide products could be evaluated in multiple Phase 1 studies. Several will proceed to Phase 2 and 3 evaluation. This large-scale trend will cost millions of dollars overall. Improved contract and grant funding from government and private sources could support the formulation, packaging, and manufacture of microbicide products for this clinical research.

Source: Microbicide Watch: An Update and Analysis of Microbicide Research and Development

Current Investment in Microbicides

In 2002, the Rockefeller Foundation conducted a major pharmaco-economic analysis of the field. It concluded that if all microbicide research leads were managed by a single pharmaceutical company, it would have to invest US \$775 million over five years to ensure the production of at least one safe, effective microbicide. This analysis considered only the costs directly related to product development, omitting other necessities like basic research, the discovery of new leads and work to assure that the products will be acceptable and accessible to users.¹⁰⁶

Funding for microbicide research and development has more than doubled in recent years, rising from US\$65 million in 2000 to US \$168 million in 2005.¹⁰⁷ In 2005 the public sector was the main source of these funds accounting for 85% of the funds invested.¹⁰⁸ The growing funding for microbicide R&D reflects a number of factors including¹⁰⁹: increased scientific confidence that it will be possible to develop a safe and effective microbicide; increased recognition of the potential role of

¹⁰⁶ *The Economics for Microbicides Development: A Case for Investment*, Rockefeller Foundation <<http://www.rockfound.org>>.

¹⁰⁷ *Adding it All Up: Funding for HIV Vaccine and Microbicide Development, 2000-2005*, HIV Vaccine and Microbicide Resource Tracking Working Group. August 2006.

¹⁰⁸ *Adding it All Up: Funding for HIV Vaccine and Microbicide Development, 2000-2005*, HIV Vaccine and Microbicide Resource Tracking Working Group. August 2006.

¹⁰⁹ *Tracking Funding for Microbicide Research & Development: Estimates of Annual Investments 2000 to 2005*. HIV Vaccines and Microbicides Resource Tracking Working Group. August 2005.

a microbicide in controlling the spread of HIV; and the entry of five products into late-stage clinical trials.

So far, microbicides development has been primarily funded by government and foundations rather than by the private industry. In March 2003, the Bill and Melinda Gates Foundation announced its commitment to make a US \$60 million grant to the *International Partnership for Microbicides (IPM)* to accelerate the discovery, development and accessibility of topical microbicides. As the largest foundation grant ever allocated to microbicide research, this money will facilitate the IPM's efforts to attract new investors and researchers to the field. Other IPM donors include the governments of Canada, the Netherlands, Ireland, United Kingdom, Norway and Denmark, Sweden the United States; the World Bank, the European Commission, the Rockefeller and the United Nations Population Fund. Commitments to the IPM are set to be US\$119 million for the period of 2002-2007.¹¹⁰

The reality is that Canada should invest a lot more in microbicides. Right now it's about USD\$5 million per year, versus USD\$15 million internationally. Norway is contributing about USD\$3.8 million, Ireland is contributing \$3.4 million – and these are much smaller countries. UK is contributing \$10-15 million per year.
(Interview #36)

The International Partnership for Microbicides (IPM) was established in 2002 to accelerate the discovery, development and accessibility of microbicides to prevent transmission of HIV. The organization's goal is to deliver a safe and effective microbicide for women in developing countries as soon as possible. IPM is focused on overcoming the four major challenges that stand in the way of microbicide development and distribution. IPM is working to: (1) accelerate product development by building production and formulation expertise; (2) build clinical trial capacity in developing countries; (3) work to establish appropriate regulatory pathways for microbicide products; and (4) plan for widespread and affordable distribution of these products.

In 2004 the United States was the only country to invest more than US\$25 million in microbicides research and development.¹¹¹ American advocates see this commitment as inadequate, pointing out that the US National Institutes of Health (which spends the lion's share of federal money in this area) is now allocating just over 2% of its total HIV/AIDS research budget on microbicide research and development. Through the Global Campaign for Microbicides and its advocacy partners, efforts to increase United States funding continue. Canada announced on World AIDS Day in 2004 that it would give \$15 million over three years to the International Partnership for Microbicides.

UNAIDS Executive Director Peter Piot has noted on several occasions that “with the current state of the art, it is likely that we will have a microbicide before we have a vaccine”.¹¹² The Rockefeller Foundation concluded in 2000 that several microbicides could have been available by 2007. Unfortunately, this was not feasible given inadequate financial commitments to microbicides research. Taking into consideration the number of potential candidate microbicides in the pipeline and the number of candidate microbicides in clinical trials, the consensus is that with sustained investment in research, development, access and advocacy, the first microbicides potentially could become available within the next seven to ten years. Success will take longer, however, if research funding remains at current levels.

¹¹⁰ International Partnership for Microbicides 2004 Annual Report. <www.ipm-microbicides.org>.

¹¹¹ *Tracking Funding for Microbicides Research and Development*. HIV Vaccines and Microbicides Resource Tracking Working Group. August 2005.

¹¹² Peter Piot, Microbicides 2000 Conference, Washington, D.C., March 13-16, 2000.

In April 2000, the Canadian International Development Agency (CIDA) in collaboration with Health Canada supported microbicides research, giving \$350,000 to Université Laval for a Phase I clinical trial of a microbicide gel that is now known as the *Invisible Condom*TM.¹¹³ Funding has also been provided to complete subsequent phases of the clinical trial.

One non-governmental organization which supports the development of microbicides is CONRAD, which has invested tens of millions of dollars in the development of a Canadian product, *UsherCell*TM, although its Phase III trials were recently halted. CONRAD is committed to improving reproductive health by expanding the contraceptive choices of women and men and by helping to prevent the transmission of HIV/AIDS and other sexually transmitted diseases. CONRAD is administered through the Department of Obstetrics and Gynecology at Eastern Virginia Medical School (EVMS) in Norfolk, VA, with its main office located in Arlington, VA. The goals of CONRAD's microbicide program are to develop new vaginal formulations that will protect women against HIV and STIs. With support from the Bill and Melinda Gates Foundation, CONRAD has provided about \$70 million to support Polydex's *UsherCell*TM.

There are so many pulls about what Canada can get involved in. CIDA is focusing on health systems, and microbicides is just not a priority right now. Facilitators would be the groundswell of support from civil society, and microbicides are consistent with our conceptual framework on how we approach reproductive health and HIV/AIDS, but not consistent with how we fund things in CIDA (country and branch specific). The way they fund things, microbicides doesn't fit. So microbicides would have to make it into country priority papers. Research in Canada for microbicides would have to come through PHAC and CIHR, but that doesn't address issues in developing countries. (Interview #11)

Canadian Institutes of Health Research (CIHR)

CIHR is the primary federal agency for health research in Canada. The Institute of Infection and Immunity (CIHR-III) is the lead CIHR Institute for the CIHR HIV/AIDS Research Initiative, which is supported by the Federal Initiative to Address HIV/AIDS in Canada. The CIHR HIV/AIDS Research Initiative is advised by the CIHR HIV/AIDS Research Advisory Committee (CHARAC). To ensure the appropriate expertise and knowledge is available to the Committee, its members represent multiple CIHR Institutes, HIV/AIDS researchers, the Ministerial Council for HIV/AIDS, the Public Health Agency of Canada and broader community organizations. This composition allows for in-depth knowledge of all aspects of Canadian HIV/AIDS research, an understanding of the complex dynamics of the HIV/AIDS community, an ability to make recommendations on research policies and programs and encourages communication between stakeholders interested in HIV/AIDS research.

CIHR has provided a total of \$2.8 million to researchers at Université Laval in support of an early phase clinical trial to evaluate the tolerance and safety of the *Invisible Condom*TM in healthy volunteers in Africa. It has also funded a number of other microbicide related research grants focused on issues such as mucosal immunity and identification of potentially protective mechanisms and substances.

In 2006, CIHR announced six priorities for the CIHR HIV/AIDS Research Initiative that will guide its investments over the coming years. The priority *Prevention Technologies and Interventions* highlights the importance of further research on microbicides. Following identification of the priorities, the Institute of Infection and Immunity has launched strategic research programs in order to advance research and create capacity in the priority areas. In December 2006 a Request for Applications in

¹¹³ S. Black, C. Armstrong, Report of the 2nd Canadian Microbicides Symposium.
<http://www.acpd.ca/pdf/micro_sym_report_en.pdf>

the area of novel HIV prevention strategies was launched, which encouraged the submission of and made funding available for microbicide projects. Nine HIV prevention grants are now being funded through this program including one microbicides related project. Microbicides research remains eligible for CIHR funding and is encouraged in the open grants and awards competitions through Priority Announcements.

Summary of CIHR Investments in Microbicides Research						
	2001-02	2002-03	2003-04	2004-05	2005-06	2006-07
Research Grants	85,643	461,791	1,469,237	2,422,917	541,228	541,228
Training and Salary Awards	28,390	26,438	20,500	0	0	0
Workshops/Symposium	0	0	0	5,000	0	0
Total Investment (\$)	114,033	488,229	1,489,737	2,427,917	541,228	541,228

What the UK Government has done - Support for microbicides

The United Kingdom has committed to provide £50 million for research and development since 1999, including for large clinical trials in Southern African countries. This is part of a funding program of £1.5 billion over the 2005-2009 period to the campaign against HIV/AIDS. Among its contributions, the UK has provided a:

- Five-year grant of £16 million to the Microbicide Development Programme, involving centres in five African countries, and coordinated by the Clinical Trials Unit of the MRC, and Imperial College London.
- Four-year grant of £1.2 million (2002-06) to the International Partnership for Microbicides (IPM) to accelerate the discovery, development and accessibility of microbicides.
- Three-year grant of £100,000 (2002-05) to Family Health International (FHI) for microbicides advocacy and networking.
- Two-year grant of £137,000 to the Population Council to enable policy dialogue and action for microbicides development and access.

Source: "Taking Action: The UK's strategy for tackling HIV and AIDS in the developing world"

Areas of Action

1. Engage Political Leadership

Stakeholders across all sectors must work to engage political leaders to understand the value of microbicides and commit the resources needed to advance microbicides R&D. Specifically, stakeholders must:

- ensure microbicides are on the federal HIV agenda on the part of CIDA, PHAC, Health Canada, and CIHR.
- keep parliamentarians informed of microbicides issues such as new research developments.
- advise and educate relevant cabinet ministers and encourage them to include microbicides in speeches.
- ensure microbicides are discussed both externally and internally at domestic and international levels.
- promote policy positions that support an approach to HIV prevention based on cultural and gender analysis and sexual and reproductive health and rights.

2. Develop a Comprehensive Investment Plan

- Canada should convene a scientific panel for microbicides spanning expertise in basic, clinical, and social-behavioural science, to set investment priorities for microbicides.
- Identify specific research competencies in Canada and work with research institutions (e.g., IPM and CONRAD) to identify areas for investment in Canadian research programs.
- Canadian efforts to integrate HIV/AIDS and STIs should continue and be used as leverage for microbicides funding.
- Although the bulk of resources is needed in the area of basic and clinical science, funding must also be allocated to social and behavioural science, community mobilization, community-based research and program initiatives, international and domestic research, capacity building and education initiatives, and across target populations and sectors.
- Funding for research should maintain a pipeline of candidate concepts and products that allows for innovations in testing proof of concept, supporting concepts with promise to subsequent testing phases, and pushing the top few products into clinical research.
- Specialized funding should be available to community-based organizations to focus on microbicides education, community-based research and advocacy.
- Support ongoing opportunities and fora for cross-sectoral discussion on microbicides.

We need to provide workshops at community events and conferences to provide education and dispel myths about microbicides. Cultural implications need to be addressed - if we promote women using microbicides covertly, men will resist and will be concerned about reduced pleasure. Canada is seen as the country which engages the community best in HIV/AIDS discussions, and it promotes good principles of community engagement. We can also build capacity of organizations in the south, women's groups to reduce their marginalization and champion human rights. Canadian funding needs to contribute domestically and internationally for community engagement. Funding should be for IPM as well as R&D in Canada. IPM funding is for R&D internationally, but doesn't include community engagement work. (Interview #30)

3. Increase Public Investment and Scientific Interest in Microbicides

Increased and targeted public-sector investment is essential in order to accelerate R&D, generate more interest in the scientific community, and support the research necessary to provide industry with evidence of effectiveness. Specific action is needed to:

- Increase awareness and commitment to microbicides within the international financial and development community, governments, and donor agencies, and encourage these public funding bodies to increase investment in microbicide research and development. This will require greatly expanded advocacy and, specifically, evidence of potential cost-effectiveness, analysis of current levels of funding and of investment required to move forward, and streamlined mechanisms to attract and disburse funds.
- Stimulate demand for increased investment in microbicides from developing-country policymakers, and from women's health groups, HIV/AIDS organizations, people living with HIV/AIDS, and potential consumers in developed and developing countries.
- Generate more interest and legitimacy within the scientific community and attract additional scientific talent to microbicide research and development, through increased funding, mechanisms to promote scientific collaboration and information exchange, and fast-track funding procedures.
- Generate additional and more flexible funding focused on product development, to follow up product leads and move promising candidates through large-scale clinical trials that don't

necessarily have to be conducted in Canada. Develop agreed-upon criteria for determining how available funding and trial sites should be prioritized.

- Provide support for identifying and strengthening the capacity of appropriate trial sites and building the necessary infrastructure with developing-country partners.
- Encourage dialogue among public funding agencies, research institutions, and the biotechnology and pharmaceutical industry. The Eurovac project, which brings together research expertise and industry in Europe for vaccine development, offers a useful model.
- Identify particular niches for Canadian researchers and civil society so that domestic research is supported along with global efforts.
- Allocate CIDA funding for stocking products for distribution of microbicides in developing countries once they are available. Explore mechanisms for advance market commitments to purchase future products as a means of providing incentives to researchers and producers.

4. Stimulate Industry Investment in Research and Development

Attracting industry investment in microbicide research and development will require efforts to improve and share market information, clarify regulatory requirements and create a more supportive regulatory environment, and develop strategies to stimulate markets and reduce legal liability risks.

Government and industry should collaborate in the following specific actions:

- Accelerate clinical research to provide proof of concept – provide evidence to convince industry that microbicides can be effective against HIV and other STIs.
- Increase industry awareness of microbicides, including setting the stage for future private-sector production, delivery, and marketing.
- Create fast-track mechanisms for streamlining research, development, and commercialization.
- Provide information about potential markets in developing and developed countries, by taking into account both public and private demand.
- Explore new sources of investment, including venture capital concerns that specialize in pharmaceuticals.
- Establish public-sector mechanisms to provide incentives for industry and support market development through, for example, international market guarantees and bulk procurement. The World Bank, among other public-sector agencies, should take the lead in this area.
- Create supportive environments that stimulate research. For example, research on policy incentives led microbicide and HIV vaccine advocates to collaborate on introduction of tax credit legislation, to encourage companies, especially small companies, to stay in the field, and to attract new companies. Another example is the Canadian government providing seed grants to pharmaceutical companies to create a product, with the condition that the companies pay back 10% of profits for reinvestment into other seed grants after a set amount of time.
- Promote collaboration among scientists, regulatory bodies, industry, and researchers to define “acceptable” levels of effectiveness, recognizing that the perfect product will never be available and that there will be successive generations of products.
- Develop internationally agreed-upon regulatory requirements for licensing different types of microbicide products and, for example, specifying conditions for over-the-counter products. Develop partnerships between regulators and associations representing industry, brokered by public agencies, to address regulatory, licensing, and related issues.
- Consider how existing mechanisms, such as Trade Related Aspects of Intellectual Property, can be used to protect patents in developing countries, and draw on the experience of organizations such as the International Partnership for Microbicides

- Assess how existing mechanisms, such as medical injury compensation funds, could be used to reduce the risk of legal liability, a particular concern for companies likely to seek a market in North America. Review other potential strategies for reducing the risk of litigation, including consumer education and counseling, clear and accurate labeling information, and post-marketing surveillance.
- Assess the likely costs and requirements of establishing manufacturing capacity, as well as the potential for technology transfer and developing-country production.

5. Develop an Interdepartmental Coordination Mechanism

One challenge in the Canadian funding environment for microbicides is the lack of coordination between the various government departments which should be investing in microbicides. The United States has created a bill called the “Microbicide Development Act” which aims to strengthen and coordinate the federal government's microbicide research and development efforts by formally establishing and authorizing microbicide programs and also establishing clear lines of responsibility at and across the three major agencies undertaking work on microbicides (NIH, CDC and USAID).

This is a model that could be transferred to Canada. At present in Canada, as in the US, microbicide funding falls under several departments with no single line of administrative accountability, no specific funding coordination, and highly variable levels of interest and commitment across institute leadership. Canada needs a coordinating body that would recruit funding from government for R&D and manufacturing, develop policies and research priorities, support community capacity building and engagement, and promote microbicides from invention, to production, development, testing, and marketing.

The mandate of this coordinating body could include:

- plan microbicides funding allocations for the next 5-10 years as part of CIDA, PHAC, Health Canada, IDRC and CIHR HIV funding programs.
- explore funding possibilities with the Global Health Research Initiative, CANFAR, CAHR, the Canadian Women's Health Network and the Centres of Excellence for Women's Health¹¹⁴.
- ensure funding across the full range of science from biomedical to psycho-social research.
- assign staff resources to monitor and implement the CMAP.
- link with the HIV Vaccines Plan and the Canadian HIV Vaccines Initiative.
- set priorities for microbicides-related calls for proposals for research, policy development, community-based projects, etc.
- strategize on how to communicate with current government to ensure that microbicides, and HIV/AIDS in general, are given adequate investment.

6. Explore Innovative Financing Systems

- Given the difficulty of stimulating industry investment in microbicides research and development, the government should explore innovative models of public investment that provide incentives to pharmaceutical companies, while at the same time ensuring affordable products and sustainable funding structures.

¹¹⁴ Atlantic Centre of Excellence for Women's Health, British Columbia Centre of Excellence for Women's Health, Canadian Women's Health Network, Centre of Excellence for Women's Health - Université de Montréal Consortium, National Network on Environments and Women's Health, Prairie Women's Health Centre of Excellence.

Clearly there has to be public investment. Issuing patents is bestowing a big privilege to pharma companies, so there should be strings attached to those lucrative patents, to ensure that the pharma companies also have to invest in microbicides research. Like in Toronto, if a film company wants to shoot a film in a neighbourhood, they are asked to invest in revitalizing a heritage building. (Interview #11)

Ideally, a researcher who discovers an HIV drug gets the patent, and then the government gives the license to industry, but on the condition that they make it available to poor countries. (Interview #20)

7. Market Studies

- Market studies are needed to provide evidence to compel investment by government funders and the pharmaceutical industry. These studies would measure the potential market demand both in developing and developed countries, and model the economic benefits for pharmaceutical manufacturers.

2. Basic Science, Clinical and Social Research

Recent Progress in Microbicides Research and Product Development

Microbicide research is increasingly considered a legitimate scientific field. Basic science is growing on issues critical to microbicide development and testing, such as sexual transmission of HIV and other pathogens, vaginal ecology, and appropriate in vitro assays and animal models. The prospects for product development are encouraging and the number of researchers and approaches is growing. Five years ago, only a handful of researchers were working on microbicides. Today, according to the Alliance for Microbicide Development, which monitors product research and development, 38 small biopharmaceutical companies, 28 nonprofit research entities, and six public-sector agencies are working on microbicides¹¹⁵. In 1994, a dozen compounds were in the preclinical stages of development, with just eight ready for early Phase I safety trials and none ready for later trials of product efficacy. In contrast, in 2006 over 60 product leads are in development, of which 10 are in later-stage clinical trials.¹¹⁶ Despite this progress in expanding the number of products being developed, they are not moving into expanded clinical testing quickly enough; almost three dozen potential products remain paralyzed in some stage of preclinical testing.

Critical issues in basic science include understanding mechanisms of transmission of HIV and other STIs during sexual intercourse, so that microbicide research can be targeted more effectively; expanding capacity for preclinical analysis of potential products; developing better animal models, including standardised assay methods to compare the potential efficacy of various candidate microbicidal compounds; generalizing from efficacy in vitro and in animal models to clinical testing; and improving understanding about bioadhesion, retention, and distribution in the vagina, and about optimal formulations and dosages.¹¹⁷

Another basic science challenge is the development of ARV-based microbicides which are effective against multiple strains of HIV. While HIV subtype C is largely predominant in southern and eastern Africa, India and Nepal, has caused the world's worst HIV epidemics and is responsible for around half of all infections, subtype B has historically been the most common subtype/CRF (circulating recombinant form) in Europe, the Americas, Japan and Australia. Subtype B is spread mostly by homosexual contact and intravenous drug use (essentially via blood), while subtype C and CRF A/E tend to fuel heterosexual epidemics (via a mucosal route). Whether there are biological causes for the observed differences in transmission routes remains the subject of debate. Most current HIV-1 antiretroviral drug regimens were designed for use against subtype B, and so hypothetically might not be equally effective in Africa or Asia where other strains are more common. At present, there is no compelling evidence that subtypes differ in their sensitivity to antiretroviral drugs. However, some subtypes may occasionally be more likely to develop resistance to certain drugs. In some situations, the types of mutations associated with resistance may vary. This is an important subject for future research.¹¹⁸

The development of an ARV-based microbicide is affected by the range of virus subtypes as well as by the wide variety of human populations who need protection and who differ, for example, in their

¹¹⁵ Microbicides Fact Sheet 13: *Trials Watch*: Microbicides in late clinical development (May 2007). <<http://www.global-campaign.org/clientfiles/FS13-TrialsWatch-May07.pdf>>

¹¹⁶ *ibid* 117.

¹¹⁷ The Case for Microbicides: A Global Priority WHO Fact Sheet No 242 *Women and HIV/AIDS*, June 2000. <<http://www.who.int>>

¹¹⁸ AVERT (2006). Introduction to HIV types, groups and subtypes. <<http://www.avert.org/hivtypes.htm>>

genetic make-up and their routes of exposure to HIV. Inevitably, different types of candidate microbicides will have to be tested against various viral strains in multiple trials, conducted in both high-income and developing countries. For Canada to have confidence that microbicides will provide effective prevention for Canadian populations, it is important that clinical trials are conducted in Canada.

For the past two years, a group of donors in the microbicide field have gathered regularly to discuss status of and challenges in the field. This group, known as the Microbicide Coordinating Board asked the Alliance for Microbicides Development to coordinate a series of meetings and working group discussions to identify the main bottlenecks that are delaying the development of microbicides and to recommend ways and means for overcoming them. The resulting analysis, entitled the Microbicide Development Strategy (MDS) is a result of a series of working group meetings and correspondence over the course of eight months in 2005. The working group consisted of leading researchers and donors who focused on four parts of the field: basic science, clinical trials, manufacturing and formulation, and finally, commercialization and access. It has been noted by civil society that a major gap in the development of the MDS is that virtually no advocates and community groups have been involved in the development of the document. As a result, a mapping exercise was carried out in 2006. Key organizations working in microbicides research, development and advocacy were invited to describe their activities with the framework of the priority gaps and actions within the MDS. This companion document entitled "Mapping the Microbicide Effort" was released in December 2006.¹¹⁹

Overview of Clinical Research on Microbicides

To be successful in reducing HIV and STI transmission at a population level, microbicides will have to be widely accepted and available. In order to be widely accepted, they will have to be non-toxic and well tolerated, odourless and colourless, easily administered, and cheap to manufacture. All of these issues of efficacy can only be assessed through rigorous clinical trials. Over the next five years, new data will be generated from clinical trials in the United States, Europe, Africa and Asia about possible efficacy of five different experimental microbicide products against HIV and other STIs. At least a dozen other microbicide candidates will soon be brought into early clinical testing, and perhaps 40,000 to 60,000 women and men will be asked to enroll in new large-scale efficacy trials. A robust and long-term clinical evaluation effort is now a priority for the microbicide field.¹²⁰

Beyond the issues related to numbers, products and participants, and dollars and data-points, there are six key aspects of clinical research that have important implications for policy over the coming years: building infrastructure for clinical trials; managing communications; developing surrogate markers of adherence and behavior; evaluating combinations of products and mechanisms of action; evaluating products for multiple uses; and ethics.

Very little microbicides clinical research has occurred in Canada. In 2002, 47 women and 23 male sexual partners participated in a Phase I clinical trial of the *Invisible Condom*TM. This trial was conducted by the Infectious Diseases Research Center of Université Laval in Canada.¹²¹ This clinical trial looked at physical acceptance and tolerance to the product in healthy women and their sexual partners. A Phase I/II trial of the *Invisible Condom*TM started in Cameroon in 2004 and is expected to be completed in 2006. There is a general consensus that conducting a Phase I trial in a developed

¹¹⁹ <http://www.global-campaign.org/GCNews.htm>

¹²⁰ Microbicide Watch: An Update and Analysis of Microbicide Research and Development

¹²¹ J. Bowcut, *Microbicide Research and Development – Products Database*, Alliance for Microbicide Development, May 2003.

country will add credibility to subsequent research efforts in developing countries.¹²² No other microbicides trial has been conducted in Canada, and none are currently planned.

In most cases, large scale Phase III microbicides clinical trials are conducted in developing countries, for political, economic, scientific and practical reasons. It is best to conduct trials and engage communities where the need is the greatest. In addition, it is more efficient to conduct such trials in settings with a high incidence of HIV infection to ensure valid results are obtained faster. Microbicides need to be tested in populations where women have high infection rates and where HIV transmission is predominantly through sexual contact. In other words, where annual infection rates are high, trial organizers can determine more quickly whether a product works, and by using fewer participants.

In clinical research the cost, complexity, and length of Phase II and III trials are key constraints. It is important to continue to explore new and innovative approaches to streamlining trials while maintaining the highest ethical standards. Trial sites must be in areas of high HIV incidence where there is a strong research infrastructure. This limits the number of potential sites and calls for efforts to identify and strengthen the capacity available at additional study sites. To meet ethical standards, participants must receive safer-sex counseling, condoms, and STI treatment; the optimum mix and approach to these services needs further exploration and refinement, and clearer guidelines for standards of services and care are needed. It is critical to use the limited resources available to test the most promising products, and developing criteria and a system to select products for testing is a priority, as is developing standardized outcomes for assessing safety and efficacy. More information is needed about the effect of other intravaginal products on microbicide safety and efficacy; the effect of microbicides on tests to diagnose STIs; the potential benefits of microbicides combined with barrier methods that protect the cervix; and possible side effects of long-term use and of use during pregnancy.¹²³

There are three phases of clinical trials:

Phase One trials determine the safety of the product when used by a small number of healthy, low-risk women over a few weeks.

Phase Two trials also test the safety of the product, this time in a larger number of women, some of whom may have higher risk factors, over a longer period of time. Some preliminary data about efficacy and acceptability of the product may be collected.

Phase Three clinical trials enroll thousands of people in several sites, and measure whether or not the microbicide actually works to prevent HIV and STIs. Some Phase Two trials of microbicides can “roll into” Phase Three trials as long as the data show good results.

Source: Global Campaign for Microbicides (July 2007). Fact Sheet #3: Microbicide Research & Development: *What's in the Pipeline?*

After microbicides are brought to market, it will be important to continue gathering information especially with regard to potential long-term side effects and possible interactions with other devices and contraceptives. This stage of trials is often referred to as Phase IV post-marketing surveillance. Health Canada should consider developing a strategy for Phase IV post-approval trials of microbicides.

¹²² D. Thompson, *HIV Vaccines in Canada: Legal and Ethical Issues: A Backgrounder Paper* Canadian HIV/AIDS Legal Network, 2001.

¹²³ The Case for Microbicides: A Global Priority. Second Edition, 2001.

<http://www.microbicide.org/microbicideinfo/reference/case.for.microbicides.2001.pdf>

Current Challenges in Clinical Research on Microbicides

Surrogate Markers to Evaluate Safety¹²⁴

One of the major causes of delay in the evaluation of microbicides in clinical trials has been the lack of validated surrogate markers that correlate with clinical findings. Outcomes from the clinical trials of Nonoxynol-9 underscore the need for rigorous safety evaluation; however, no reference standard exists that predicts ultimate safety in vitro, in animal, or in early clinical models. Currently, clinical safety testing utilizes pelvic examinations and colposcopy to evaluate patients for signs of macroscopic and microscopic irritation, inflammation, and ulceration. In an effort to standardize colposcopic assessments by multiple practitioners, study sponsors have developed common staff training, have shared multimedia resources for the description of epithelial lesions, and have emphasized receiving second opinions when clinical findings are noted.

Efficacy and Trial Design¹²⁵

In order to reliably test microbicide safety and efficacy, it is necessary to conduct large-scale clinical trials that include thousands of HIV-uninfected, high-risk women who will be randomized to active or placebo formulation and followed for several years. In reality, because women and their partners may be unaware of their HIV status, HIV-infected women should be studied in early clinical trials. The need to establish standards of care and informed consent is challenging in resource-poor countries and communities where access to health care is extremely limited. Recent HIV prevention trial controversies underscore the need for greater international consensus on study design and long-term follow-up and for sensitivity in dealing with scientific, technical, and local political issues.

Trial populations must be identified with an HIV incidence of at least 2% if sample size is to be feasible. However, this high level of HIV transmission must be vigorously addressed through prevention counseling, screening for and treatment of STIs, and provision of condoms and health education. Further, non-vaginal exposure to HIV such as through frequent anal intercourse or the use of non-sterile needles, will reduce the effect of a microbicide. Thus, considerable behavioural data will need to be collected at these phase III trials for the results to be interpreted and understood correctly.

One of the persistent concerns of microbicide development is that offering access to a partially effective microbicide might offset successful condom promotion efforts¹²⁶. To address this concern, in 2003, a US Food and Drug Administration advisory committee recommended that efficacy trials should include an additional randomized study arm for patients to receive only condom counseling. This recommendation has led to debate about the effect of an unblinded control (i.e., condom-using participants) on study reliability, and the requirement for increased recruitment and resources. Mathematical projections suggest that a low-efficacy microbicide used consistently would provide greater protection over time than a less consistently used, high-efficacy product, such as a condom.

¹²⁴ Darpun Dhawan¹ and Kenneth H. Mayer. *Microbicides to Prevent HIV Transmission: Overcoming Obstacles to Chemical Barrier Protection*. JID 2006:193 (1 January)

¹²⁵ *ibid* 126

¹²⁶ *ibid* 127

Expense¹²⁷

Phase III trials are large, requiring multiple sites in high-incidence regions, long in duration and hence expensive. Phase III trials of novel microbicide products undertaken in resource-poor regions in large numbers of women are financially challenging, inevitably costing upwards of \$US50 million depending on sample size. In the absence of commercial investment, this burden falls on the charitable and/or public sector. It is highly likely that because of the high costs, phase III trials will be the major cause of delay in new product development and testing.

Difficulty Controlling Adherence¹²⁸

Adherence to use of the microbicide will be central to phase III trials' successful outcome, and these agents will need to be used to protect every risky act of intercourse. As with male condoms, adherence is unlikely to be complete, and may reduce over time. Thus, trials designed to assess proof of efficacy should be for as short an intervention period as possible in order not to dilute any antiviral effect of the microbicide through the likely reduction in adherence over time.

In the long term, the effectiveness of microbicides will be highly dependent on continued high-level adherence, and this will need to be examined in longer term trials. In addition, clinical trials need to incorporate methods to improve the reliability of self-reporting by trial participants regarding their level of adherence to the microbicide being tested. As the safety and tolerability of these new materials will continue to be paramount, some participants even in shorter trials will need longer follow-up for safety. Ultimately, it is possible that adherence could be enhanced through novel methods for the sustained delivery of microbicides within the vagina without the need for dosing prior to each act of intercourse. For example, the development of vaginal rings allowing sustained slow release of the active agent over weeks or months would overcome the key issue of adherence.

Community Mobilization and Capacity¹²⁹

Clinical research is conducted largely at small hospitals and health clinics, far from the conference centers and headlines of global health policy. On these frontlines of AIDS research, capacity is needed to support the research participants who are helping to assess the safety, acceptability, and potential efficacy of candidate microbicides.¹³⁰ The "community" is defined as those involved in trials, as well as the population at large, including NGOs and advocates that are serving that population. A vital ingredient for the success of clinical trials is building community capacity to understand the value of microbicide trials, to provide information to participants, to participate in ethical negotiations that arise from clinical trials, to ensure standard of care for trial participants who become HIV-positive during the trial, and to ensure informed consent.

Common challenges involved in conducting trials include ethical issues and community preparedness. Prevention and treatment trials face common volunteer recruitment and retention challenges. Advocates have developed expertise that should be shared regarding new mechanisms for community participation in trial processes, such as developing locally owned participants' Bills of Rights. There are common needs relating to training to support community participation in advisory,

¹²⁷ *Phase III Trials of Vaginal Microbicides* in Jonathan Weber, Kamal Desai, Janet Darbyshire, on behalf of the Microbicides Development Programme. *The Development of Vaginal Microbicides for the Prevention of HIV Transmission*. PLOS Medicine. May 31, 2005. <<http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0020142&ct=1>>

¹²⁸ *ibid* 129.

¹²⁹ Anna Forbes at 2nd Canadian Microbicides Symposium. <http://www.acpd.ca/pdf/micro_sym_report_en.pdf>

¹³⁰ Microbicide Watch: An Update and Analysis of Microbicide Research and Development

ethical monitoring and management structures. Communities would benefit from more integrated approaches to community education about the nature of different prevention and treatment products being trialed.¹³¹

Much work has been done in the last few years to define ethical issues specific to conducting research in developing countries. Efforts are required to further develop ethical practices and standards that take into account local cultural contexts. Issues to be considered include informed consent, confidentiality, compensation, use of placebos in trials, and the standard of care for any trial participants who require HIV-related treatment and care. Because standard of care, best proven prophylaxis and access to post-trial health services, vary widely between countries, national guidelines on treatment and care need to be established. Mutual benefits would be gained from sharing approaches adopted in prevention and treatment trials to resolving these issues.¹³²

The most common mechanism for promoting community involvement at microbicide trial sites in both developing and developed countries is a local Community Advisory Board (CAB). Engaging a wide range of stakeholders, including people living with HIV/AIDS, as active and informed partners in decision-making about the research and its implementation can enhance both the scientific process and ethical integrity of clinical trials. CABs are one structure through which individuals impacted by HIV can use their unique knowledge to provide input on the community relevance, scientific merit, ethical parameters, and practical feasibility of HIV vaccine trials. CABs were established in each of the three Canadian sites for preventive HIV vaccine trials (Vancouver, Toronto and Montreal). There are several potential benefits of establishing CABs:

- CABs can be very effective in helping the researchers understand the target communities. They can also help recruit and retain trial participants and disseminate information in the community.
- CABs can assume a leadership role in the design of the informed consent process, in the disclosure of information to participants, and the review of information materials.
- CABs formed by volunteers and community activists can provide a forum for trial participants to raise issues and concerns.
- CABs can engage researchers substantively on issues of concern.
- CABs can help to ensure good working relationships between trial organizers, researchers and local health services.
- In case of multi-location trials, different CABs should be encouraged to exchange information and ideas.
- CABs can help to disseminate results of the trial to the community

When things blew up over the Tenofovir trials, it was very painful and costly, activists went too far and they didn't get the help or attention that was merited. The activists never meant the trials to die, but they wanted to voice their concerns. One of the things that we have to work on is how do we in clinical trials pay attention to concerns about community and trialists to ensure that dialogue is happening. We need to get media and trialists to keep talking, so when an issue arises or recruits are raising questions, they don't go directly to the press, but have someone running the trial listen to their concerns.
(Interview #38)

Some of the issues in microbicides research and clinical trials that should be addressed at the community level are outlined below.

¹³¹ Canadian HIV/AIDS Legal Network (2004). HIV Treatments, Microbicides and Vaccines: Developing an agenda for action — Background Paper. <<http://www.aidslaw.ca/publications/publicationsdocEN.php?ref=360>>

¹³² *ibid* 133.

Access to Clinical Trials. Vulnerable communities should be well represented in any clinical trial. For example, women have been historically excluded from participation in many clinical trials because of concerns over the possibility of pregnancy. However, microbicides trials are predominantly conducted in women because they would benefit most from future microbicides. Pregnancy is still an exclusion criterion for participation in the first generation of microbicide trials. However, women from all parts of society should have access to trials, including young women, women from Aboriginal communities and other ethnocultural backgrounds and women who use drugs. Potential microbicides should also be tested for rectal and oral use in both men and women. Inclusion of other vulnerable populations (such as persons who use drugs, for example) must also be considered.

Informed Consent. In Canada, most HIV researchers are encouraged to use the model consent form developed by the *Canadian HIV Trials Network* to ensure that trial participants are fully informed of their rights. Nonetheless, these consent forms can be quite complex and time-consuming. With regard to the *Invisible Condom™* Phase I trial, the Review Ethics Board of Université Laval reviewed the informed consent form to ensure that participating women and their partners had made an informed decision when they enrolled in the trial. This consent form was reportedly six pages long.

Informed consent is an ongoing process and researchers should inform participants of new information as it arises during the trial. Alternate methods for obtaining informed consent should also be made available to individuals with low literacy skills. To ensure that consent is truly informed, researchers are encouraged to work closely with community representatives.

Standard of Care. Any individuals who become infected with HIV during their participation in a microbicides clinical trial should be provided with life-long, optimum standard of care for HIV.

Suspicion and Sigma. Some communities are suspicious of clinical trials. For example, Aboriginal communities in Canada have often been the object of scientific health-related investigation where there have been violations of research ethics. There is also widespread suspicion among community leaders, especially in lower income countries and in disadvantaged communities which can be vulnerable to being used as “guinea pigs.” In addition, stigma is still attached to participants taking part in HIV/AIDS clinical trials because they are perceived, by virtue of association, to be living with or at risk of HIV/AIDS. This issue might be of particular concern in small and marginalized communities. Communities can engage in educating their members about microbicides and related trials, and work towards reducing HIV-related stigma and discrimination.

Access to the results of the trial. Using the same argument as in the UNAIDS guidance document on vaccine research, one can suggest that any microbicide demonstrated to be safe and effective, as well as other knowledge and benefits resulting from microbicides research should become available to all participants of the trials as soon as possible.¹³³

I've learned a number of lessons about involving community, to make sure that they understand what the study is about or not about, handling expectations, rapid communication if a study encounters a problem, but also the study must be seen to be prudent to begin with, establish relationships of trust. (Interview #34)

¹³³ See Guideline 2, UNAIDS, “Ethical Considerations in HIV Preventive Vaccine Research,” *UNAIDS Guidance Document*, 2000.

Understanding Behaviours

There are many social and behavioural issues that will accompany microbicides trials and testing, education and distribution, and social research can help elucidate some of these issues. Complex issues arise in microbicides trials in ensuring that use of microbicides is not accompanied by a reduction in the use of condoms. As with vaccine trials and HIV/AIDS treatment trials, there are concerns that microbicides trials may generate undue optimism among members of the community, who may regard microbicides as surefire HIV/STI prevention. This phenomenon, often referred to as “therapeutic misconception,” may result in a heightened tolerance for risk-taking. This can occur in contexts where clinical trials are happening, but also potentially in any context where information about the progress of microbicides research is made available. Experience shows that the possible effects of unfounded microbicide or vaccine optimism resulting from clinical trials can be countered through strong community education efforts. Together with researchers, community members can help to avert unfounded optimism by emphasizing prevention.¹³⁴

Social research should accompany clinical trials to inform decisions about licensing new products and so that educational strategies can be developed to counter any adverse behavioural consequences of the introduction of new products. An issue being confronted by all three fields – HIV/AIDS treatment, vaccines and microbicides research – is the impact on behaviour of the introduction of new products. There is a concern that people may increase their risk taking behaviours if they know that they have access to treatments or a vaccine, or if they are using a microbicide. If this is a common behavioural response, it would reduce the benefits of these products in fighting the epidemic.¹³⁵

We need a better research program for women and HIV research. I would like to see women not so neglected in research. Women's issues generally are not addressed in HIV/AIDS research, so we need to give researchers incentives to focus on women's issues. We need to change the priorities of government, change their mentality. (Interview #8)

Stimulating Interest in Women's Health

Research into prevention options for women has been a marginalized issue among policy makers, programmers, and donors. This may be due to long-standing provider bias against barrier methods in family planning programs, or to general discomfort with interventions that specifically focus on sexuality. There is a general perception that women living in conservative societies will not use vaginal methods, though this assumption has been disputed by research¹³⁶. A lack of information about these methods has led to an excuse for inaction. Action-oriented research can help make the case for the need for investment in the development of microbicides, providing the evidence for the barriers facing women currently with respect to HIV/STI prevention, the potential benefits of a female-controlled method and the practical issues of microbicides promotion, education and use.

Population-Specific Issues in Canada

There is a perception that microbicides are targeted to the developing world, however there are many Canadian women and men who equally could benefit from microbicides. Several social research questions need to be addressed¹³⁷ with respect to ensuring culturally-appropriate education

¹³⁴ The Case for a Microbicides Action Plan.

¹³⁵ Canadian HIV/AIDS Legal Network (2004). HIV Treatments, Microbicides and Vaccines: Developing an agenda for action — Background Paper. <<http://www.aidslaw.ca/publications/publicationsdocEN.php?ref=360>>

¹³⁶ Interagency Coalition on AIDS and Development (2004). HIV/AIDS and Prevention Options for Women Fact Sheet. <http://www.icad-cisd.com/content/pub_details.cfm?id=23&CAT=9&lang=e>

¹³⁷ Report of the 2nd Canadian Microbicides Symposium. <http://www.acpd.ca/pdf/micro_sym_report_en.pdf>

and access to women, prison populations, Aboriginal peoples, people who use injection drugs, gay men and other men who have sex with men, people of African or African-Caribbean descent, youth and people living with HIV. Organizations which work directly with these community groups should take a lead in building awareness of microbicides amongst their community members, and partner with social scientists to investigate cultural understandings of microbicides use. The social and behavioural research needed for understanding microbicides acceptance amongst specific target populations is best conducted through inter-sectoral research teams comprised of community-based HIV/AIDS organizations, women's sexual and reproductive rights organizations, sexual behaviour researchers, and women's health researchers.

There are concerns around community trust and skepticism amongst communities that have historically been colonized or experienced slavery – that historical perspective plays a big role in how these products are perceived (e.g., strong memories of the Tuscegee study), and there's the same distrust in Aboriginal communities. They'll say: 'why should I trust that this is for my own good?' (Interview #16)

Areas for Action

1. Map out Canadian Research Abilities

Stakeholders, including researchers currently engaged, or interested, in microbicides research, research funders and professional societies, should collaborate to map out Canada's research landscape through the following actions:

- identify researchers interested in microbicides from the fields of basic science, clinical trials, epidemiology, behavioural science and social science.
- maintain an inventory of all microbicides-related research occurring in Canada (both for vaginal and rectal use).
- identify where research is taking place at the levels of individual scientists and their research programs, hospitals and laboratories, and global partners.

2. Advocate for Investment in Microbicides Research

Research activities in basic science, clinical trials, epidemiology, behavioural science and social science should receive adequate and sustained funding.

Actions should include:

- build awareness of microbicides within research groups, pharmaceutical companies, community-based organizations and government departments.
- engage more HIV researchers outside of basic science and identify their potential contributions in terms of understanding and addressing access issues, processes of roll-out, impact on communities and gender issues.
- explore ways to facilitate Canadian researchers linking to research priorities of the IPM and the Microbicides Development Strategy (being developed by the Microbicides Coordinating Board, that was released in Toronto at the International AIDS Conference (August 2006).
- facilitate private-public partnerships between researchers, government and the pharmaceutical industry.

If the money is there, the science will follow. (Interview #36)

3. Develop Partnerships

Researchers currently engaged, or interested, in microbicides research, research funders and professional societies should work together domestically and with international partners to:

- identify opportunities for partnerships between researchers, with pharmaceutical companies, community-based organizations and government departments.
- convene regular microbicides research meetings for mutual learning and to advocate for investments.
- link with HIV vaccine research initiatives, community-based organizations, small and large pharmaceutical firms, international NGOs, and multilateral organizations (e.g., UNAIDS).
- facilitate learning and collaboration between microbicides researchers and those conducting research on gynecology, HIV vaccines, antiretroviral treatments, pre-exposure prophylaxis, the female condom and other female contraceptive devices, STI prevention, sexual behaviours, gender issues, etc.
- research funders – such as CIHR and SSHRC – should explore mechanisms to support social and behavioural research needed for understanding microbicides acceptance amongst specific target populations.

4. Encourage Researchers to Engage in Microbicides Research

The Government of Canada's departments (i.e., CIHR, CIDA, IDRC, HC) and other funders (e.g., OHTN, CANFAR, CTN) should collaborate in finding mechanisms to sustain microbicides research and development, both domestically and globally, through the following actions:

- develop a coordinated funding mechanism between various government departments, and with the IPM to avoid duplication of effort and to find a niche for Canadian researchers.
- educate research grant peer reviewers about microbicides and their potential impacts.
- issue microbicides-specific requests for proposals.

5. Set Priorities

Stakeholders, including researchers currently engaged, or interested, in microbicides research, researcher funders and professional societies should work together to:

- identify the range of products coming into and moving through the R&D pipeline in Canada along the continuum of:
 - stage of development - from conceptual compounds in pre-clinical testing through to candidate products in phase III trials.
 - concepts in development - from non-specific barrier methods to innate mucosal immunity products, to ARV-based microbicides; and those that may or may not protect against STI infection and be contraceptive, as well as protect against HIV infection; products for vaginal versus rectal use.
- assess the research programs that are underway globally and identify particular niches in which Canadian researchers can best make a contribution.
- develop a detailed problem definition of the major hurdles facing scientists and identify mechanisms to help researchers overcome these hurdles.

- after considering the range of products and concepts in various phases of development, set priorities for investment over a specific number of years (e.g., 3-5 year plan for research priorities).

Maintaining the research pipeline is a big issue: If 20 things are going into pipeline from bench research, we're lucky to have one come out at the end. There's relentless attrition. In order to have quantity of pipeline products - through to formulation, production and cost issues...we need a broader pipeline, and a way of sorting them, killing the ones that aren't viable. In a pharmaceutical company, that happens as a matter of course. In the whole field, the challenge is who decides what goes forward, and which don't. Each funder does their own thing. The big policy decision is we need to have a global effort that fills that pipeline and appropriately invests in promising ideas. (Interview #38)

6. Build Capacity in Canada

Clinical trials expertise in Canada should be sustained and enhanced. There is an effective Canadian HIV Trials Network (CTN) that has experience conducting vaccine trials in Canada. The CTN can play a major role in conducting the trials, overseeing all the regulatory aspects of coordinating and implementing the clinical trials, conducting data analysis, and reporting the results. These roles should be adequately supported.

Canadian researchers conducting microbicides trials should seek ways to include Canadian women so that research findings will be easily transferred to Canadian contexts. Populations that should be considered for inclusion in clinical trials are Aboriginal women, African and African-Caribbean women, women involved in the sex trade, and women living with HIV.

Researchers and research funding bodies should encourage greater opportunities for training the next generation of microbicides researchers, such as through the following actions:

- provide salary support for senior scientists to target their research activities to microbicides, and scholarships and training awards to build capacity of new scientists.
- facilitate student internships to build the capacity of African, Caribbean and Aboriginal researchers.
- encourage university educators to include microbicides in basic, clinical and social science curricula.

7. Build Capacity in Developing Countries

The challenge is not only to ensure that products developed initially by Northern sponsors can be trialed in Southern hosts, but also to build capacity for Southern countries to be able to exercise greater independence in conducting all aspects of R&D within their own countries. The longer term goal needs to be comprehensive transfer of skills and technology to regional centres of excellence in the South. This imperative arises not only from pragmatic considerations, but also from international human rights norms derived from the right to share in scientific advancement and its benefits. This right is expressed in various international declarations including Article 27 of the *Universal Declaration of Human Rights*, the *UN Declaration on the Use of Scientific and Technological Progress*, the *Declaration of Commitment on HIV/AIDS*, and Paragraph 7 of the *Doha Declaration*, which affirms “the commitment of developed-country Members to provide incentives to their enterprises and institutions to promote and encourage technology transfer to least-developed country Members.”¹³⁸

¹³⁸ Canadian HIV/AIDS Legal Network (2004). HIV Treatments, Microbicides and Vaccines: Developing an agenda for action — Background Paper. <<http://www.aidslaw.ca/publications/publicationsdocEN.php?ref=360>>

Expanding the capacity of countries to conduct clinical trials is a high priority for advocates from the three fields of HIV/AIDS treatments, microbicides and vaccines. This issue is particularly pressing for prevention trials, which require thousands of volunteers. Building trial infrastructure is becoming of more central importance as more prevention products move into large scale phase III trials. Building trial site capacity in developing countries will also facilitate trials of treatment strategies designed specifically for resource-poor settings.¹³⁹ Specific areas in which capacity building should focus are in building trial infrastructures, such as training health personnel and establishing clinics.

8. Provide Leadership in Upholding Ethical Standards

Much work has been done in the last few years to define ethical issues involved in conducting research in developing countries, notably the UNAIDS vaccine ethics guidance document¹⁴⁰, the UK Nuffield Council Report, the US National Bioethics Commission report and the Guidelines produced by CIOMS¹⁴¹. International principles of ethics in biomedical research provide a starting place for designing and implementing clinical trials that ensure that the ethical principles of autonomy, beneficence and justice are upheld for trial participants and communities where research takes place. Efforts are now required to equip developing countries to apply these frameworks and to engage in consultative processes with communities to develop guidelines that take into account local cultural and legal contexts.

One area in which Canada can provide leadership in microbicides trials is in upholding and monitoring the ethical standards by which trials are conducted. This role should involve building capacity in developing countries to establish standards of care, counseling and testing, and informed consent for trial volunteers. These issues should be addressed for a variety of contexts, including those amongst women with low levels of literacy. Canadian researchers are in the process of developing a “Code of Conduct for HIV/AIDS Research Involving Civil Society”¹⁴² and have been involved in the review of ethics issues with the pre-exposure prophylaxis trials.

9. Advocate for Human Rights-Based Approach to Microbicides Research

Canada has built a strong international reputation for its human rights approach to HIV/AIDS policy, programming and research. Canada’s *Leading Together* action plan frames human rights, among other ways, as supporting HIV prevention options that can be controlled by women (e.g., microbicides), and complying with international guidelines for conducting health research. Because the social determinants of the HIV pandemic encompass poverty, stigma, discrimination, and injustice, HIV prevention research requires the enrollment of people who are often vulnerable in

¹³⁹ Canadian HIV/AIDS Legal Network (2004). HIV Treatments, Microbicides and Vaccines: Developing an agenda for action — Background Paper. <<http://www.aidslaw.ca/publications/publicationsdocEN.php?ref=360>>

¹⁴⁰ UNAIDS (2000). Ethical Considerations in HIV Preventive Vaccine Research: UNAIDS Guidance Document, Geneva.

¹⁴¹ The Ethics of Research Related to Healthcare in Developing Countries, London: Nuffield Council on Bioethics, 2002. (available at <www.nuffieldbioethics.org/publications>) Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries Bethesda, Md.: National Bioethics Advisory Commission, 2001 (available at <www.georgetown.edu/research/nrcbl/nbac/pubs.html>); International Ethical Guidelines for Biomedical Research Involving Human Subjects Geneva: Council for International Organizations of Medical Sciences (CIOMS) 2002; see also European Group on Ethics in Science and New Technologies Ethical Aspects of Clinical Research in Developing Countries Brussels: European Commission 2003.

¹⁴² J Gahagan & J Nadeau (in progress). A Code of Conduct for HIV/AIDS Research Involving Civil Society: A Tool for HIV/AIDS Research & Civil Society Sectors.

multiple ways¹⁴³. From a human rights perspective, it behooves researchers to take measures to protect these most vulnerable populations from exploitation.

10. Conduct Microbicides Research

Canadian researchers have a key role in developing and implementing a robust basic, clinical and social science research agenda for microbicides.

- Basic research would seek to address: understanding of mechanisms of transmission of HIV and other STIs during sexual intercourse; expanding capacity for preclinical analysis of potential products; developing better animal models, including standardised assay methods to compare the potential efficacy of various candidate microbicidal compounds; generalizing from efficacy in vitro and in animal models to clinical testing; and improving understanding about bioadhesion, retention, and distribution in the vagina [and rectum], and about optimal formulations and dosages.¹⁴⁴
- Clinical research is needed to address issues such as: development of validated surrogate markers that correlate with clinical findings; improvements in trial design and management of standards of care and informed consent; development of methods to control and measure adherence during clinical trials; and building community mobilization and capacity to host clinical trials.
- Behavioural research would help to understand the impacts of microbicides trials on individual behaviours, community perceptions and other social impacts. Social research would enhance understanding of: risk taking behaviours; how to counter the potential effects of microbicide optimism resulting from clinical trials or availability of microbicides in the market; barriers facing women with respect to HIV/STI prevention and the potential benefits of a female-controlled method; and the practical issues of microbicides promotion, education and use.

11. Ensure Coordination Across Clinical Trials

Canadian researchers and their funders have a responsibility to ensure that there is communication and collaboration across various technologies (e.g., malaria, HIV vaccines, tuberculosis, microbicides, pre-exposure prophylaxis) so that trial sites in developing countries aren't exhausted. At a minimum, researchers planning the trials should communicate and develop concerted efforts around establishing and strengthening conduct of clinical trials.

With respect to clinical trials, some of the ways that treatment and prevention advocates could work together are as follows:¹⁴⁵

- use laboratories, clinics, and the mobilization for ARVs as the basis for prevention trials;
- scale up treatment at prevention trial sites for participants who sero-convert and their communities;
- conduct joint community education on treatment/prevention packages;
- empower communities (e.g., sex workers and people who use drugs) to engage in community debates and decisions about trials;

¹⁴³ HIV Prevention Trials Network Ethics Guidance for Research, 2003.

¹⁴⁴ The Case for Microbicides: A Global Priority WHO Fact Sheet No 242 *Women and HIV/AIDS*, June 2000. <<http://www.who.int>>

¹⁴⁵ Canadian HIV/AIDS Legal Network (2004). HIV Treatments, Microbicides and Vaccines: Developing an agenda for action — Background Paper. <<http://www.aidslaw.ca/publications/publicationsdocEN.php?ref=360>>

- develop a regulatory and ethical review capacity, including human rights training on issues such as informed consent, confidentiality, compensation and standards of care; and
- facilitate technology transfer and South-South learning to support developing country R&D that addresses local needs.

12. Preparedness and Acceptance Studies

- Basic science and clinical research for microbicides should be balanced with and accompanied by social research, to understand how service providers should be approaching communities to participate in clinical trials and how to market the products once available.
- CIHR and other research funders should support social research that assesses the preparedness of various communities in Canada and in developing countries to provide education about, promote and distribute microbicides.
- Research funders should support social research that assesses acceptance amongst communities in Canada and in developing countries of microbicides, anticipating particular concerns, barriers and misconceptions about microbicides in order to appropriately develop, target and deliver education. Acceptance studies would also document the demand for, and willingness to use, microbicides amongst various communities in Canada and abroad.
- Ways to incorporate microbicides education and promotion in various domestic and international contexts should also be studied, in order to explore mechanisms of achieving acceptance and preparedness for microbicides without detracting from existing efforts to provide care, treatment and prevention.
- Microbicides acceptance studies among Aboriginal people in Canada should be supported by funders, researchers and community groups to allow for a greater understanding of how to introduce additional user-controlled STI prevention tools successfully in these communities.

13. Policy Development

- Policy research is needed to establish the potential cost effectiveness and impact of microbicides in HIV prevention at different levels of use and efficacy, and to determine the potential impact of introducing microbicides on condom use.
- Additional information on the size and characteristics of the potential market is also critical to help stimulate investment and determine appropriate approaches to product introduction and distribution. Information to donors is essential to stimulate an expanded financial base for microbicide research.
- Social researchers, community-based organizations and government should collaborate to develop policy and guidelines around education, delivery and access to microbicides.

14. Translating Lessons Learned

There are important opportunities to learn from other prevention and treatment technologies – such as ARVs, pre-exposure prophylaxis (PREP), the HPV vaccine, male circumcision, female condoms, and emergency contraception – and how they have been received by communities from education, usability and marketing perspectives. Specific research efforts should include studies to take stock of lessons learned from these other prevention and contraception technologies, and translate those lessons to microbicides promotion and delivery.

There are many lessons to be learned from the controversies surrounding PREP trials with the antiretroviral drug tenofovir (Viread), particularly with respect to perceived defects in trial design and implementation, and inadequate consultation with the communities involved. One of the main lessons learned was that close collaboration between researchers and activists is essential for a prevention trial. Early involvement of stakeholder groups is necessary to prevent dissent within the affected communities and to create systems to respond effectively to concerns raised during the course of the trial. Four main challenges identified in PREP trials were: 1) providing treatment and care to trial participants, 2) establishing the standard of care for prevention interventions offered to participants, 3) ensuring research literacy for potential participants, and 4) strengthening mechanisms for community involvement.¹⁴⁶

¹⁴⁶ E Mills. Tenofovir trials raise ethical issues. HIV/AIDS Policy and Law Review: Volume 10, Number 2, August 2005

3. Manufacturing, Production and Regulatory Issues

Canada's Regulatory System¹⁴⁷

The Therapeutic Products Directorate (TPD), a subdivision of the Health Products Food Branch of Health Canada, undertakes a variety of activities such as formulating policies or regulations to support its role as the federal regulatory authority for the sale of pharmaceutical drugs and medical devices in Canada. Health Canada's TPD is the national authority that regulates, evaluates and monitors the safety, efficacy, and quality of therapeutic and diagnostic products available to Canadians. These products include drugs, medical devices, disinfectants and sanitizers with disinfectant claims.

The TPD has a Priority Review Process in place which allows for a faster review to make available promising drug products for life-threatening or severely debilitating conditions, such as cancer, AIDS, or Parkinson's Disease, for which there are few effective therapies already on the market.

Prior to being given market authorization, a manufacturer must present substantive scientific evidence of a product's safety, efficacy and quality as required by the *Food and Drugs Act and Regulations*. When a product is offered for sale in Canada to treat or prevent diseases or symptoms, it is regulated as a drug under the *Food and Drugs Act*. Drugs are authorized for sale in Canada once they have successfully gone through the drug review process¹⁴⁸. Throughout the process, the safety and well-being of Canadians is the paramount concern.

The term Medical Devices, as defined in the *Food and Drugs Act*, covers a wide range of health or medical instruments used in the treatment, mitigation, diagnosis or prevention of a disease or abnormal physical condition. Health Canada reviews medical devices to assess their safety, effectiveness and quality before being authorized for sale in Canada.

If the microbicide was put onto a sponge, on a condom, in an applicator, or some other delivery system, it would most likely be classified as a medical device (as in a product like the *Invisible Condom*TM). Otherwise, it would be classified as a drug (e.g., a cream or gel), certainly if it's available only by prescription, and maybe if it's available as an over-the-counter product.¹⁴⁹

In recent years, regulators in Health Canada have been tracking microbicides research literature with attention to safety and efficacy components, in particular to rule out that the microbicide products would have undesirable side effects such as increasing localized lesions which increases transmissibility of the virus, conferrence of any kinds of drug resistance, or resulting in overgrowth of other pathogens that may be in the immediate area, e.g., *Clostridium difficile*.¹⁵⁰

Regulatory Concerns¹⁵¹

Because microbicides represent a new product category, there is no clear precedent for establishing regulatory requirements for products at different stages of research and development, determining what level of effectiveness would be required for approval and introduction, and establishing what

¹⁴⁷ Health Canada: Drugs and Health Products. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/index_e.html>

¹⁴⁸ Drug products include prescription and non-prescription pharmaceuticals, disinfectants and sanitizers with disinfectant claims.

¹⁴⁹ Information from Interview #18.

¹⁵⁰ Information from Interview #18.

¹⁵¹ The Case for Microbicides: A Global Priority WHO Fact Sheet No 242 *Women and HIV/AIDS*, June 2000. <<http://www.who.int>>

data are needed to support an application for product licensing. A related issue is uncertainty about prescribing and labeling information and possible caveats (for example, about use with condoms), which could have significant implications for product marketing and pricing. These issues have been recognised and some steps are being taken towards resolving them. For example, the US Food and Drug Administration has established a Topical Microbicide Working Group that has made a commitment to priority review of products to prevent serious and life-threatening diseases, including microbicides for HIV prevention. The working group is also committed to advising applicants about the regulatory process, working to clarify preclinical requirements, and devising other fast-track mechanisms. These mechanisms and approaches are still new and their effectiveness in helping to bring a product to market has not been confirmed. However, a similar approach could be explored with regulatory agencies in Europe, using the centralised application procedure for European Union states of the European Medicines Evaluation Agency.

Pricing and Subsidy¹⁵²

As with any new public health product category intended for the global market, microbicides also raise issues of intellectual property, pricing, and subsidy. It is critical to devise pricing mechanisms and purchase agreements to ensure that new products are available and affordable for the developing world and the public sector where they are needed most, while protecting intellectual property. Recent experience with HIV/AIDS vaccines and the IPM demonstrates that innovative partnership arrangements can help reconcile industry's interest in profit with consumers' need for expedient access to safe and affordable products.

Canada's Access to Medicines Regime

The *Jean Chrétien Pledge to Africa* Bill C-9, also known as Canada's Access to Medicines Regime, amends the *Patent Act* and the *Food and Drugs Act* to facilitate the export of lower-cost generic medicines to developing countries confronting public health problems but lacking their own capacity to manufacture pharmaceutical products. The law makes it possible for generic drug manufacturers to get "compulsory licenses" that override the patents on particular drugs so they can make generic versions for export to eligible developing countries. The Act was passed unanimously in Parliament, and received Royal Assent on 14 May 2004. The Act is accompanied by Schedule 1 which is a list of pharmaceutical products eligible for compulsory licensing for export. It will be important that microbicide products are added to this list once they become licensed in Canada as safe and effective pharmaceutical products.

Process for Applications Under Bill C-9

If a pharmaceutical company is willing to produce a microbicide and wanted to export it to developing countries, they could apply under Bill C-9. Companies which have submitted under Bill C-9 can apply for products which are currently under patent so that they can export generically. But it's up to the pharma companies to apply under Bill C-9, they will have to apply based on a request, make a Bill C-9 application to Health Canada for the exported license, and the drugs would have to meet the same safety and efficacy requirement as they would in Canada. (Interview #17)

¹⁵² The Case for Microbicides: A Global Priority WHO Fact Sheet No 242 *Women and HIV/AIDS*, June 2000.
<<http://www.who.int>>

Liability¹⁵³

Some industry executives have also expressed concern over potential risk of liability, including both litigation related to side effects and failure to protect against HIV and other STIs. While it is unclear whether liability is of equal concern for all companies and all markets, the topic warrants further examination.

Improving the Regulatory Terrain¹⁵⁴

Regulators walk a tightrope between approving products too quickly (and later discovering they do harm) and being overly cautious on safety concerns (and thus holding up approval of products that would be powerful public health tools). When they are in relatively new territory (as with microbicides), regulators tend to err on the side of safety. In terms of regulation, the main dilemma for the microbicide field today centers on how regulatory approaches can best anticipate and review product data for safety and efficacy, yet still get safe, effective products.

Developing countries are weak in terms of regulatory bodies, and if we want them to participate in research and development, we need to be sure that they have the ability to regulate the products that they're asked to sign off on. We really are so dependent on US FDA for approval of these products while people are dying like flies in developing countries. There is a terrible lag time between a product being proven efficacious, and getting it through the regulatory frameworks and to the people. How do we accelerate licensing and approval in a responsible way? We can't have 10 more years of death because of bureaucracy. (Interview #38)

Areas for Action**1. Overcoming Regulatory Hurdles**

- Canadian regulators should begin the process of investigating the regulatory frameworks under which potential microbicides would fall, depending on whether they are classified as drugs or medical devices. Hurdles within those regulatory frameworks should then be addressed and barriers removed as much as possible, in order to ensure rapid review and approval once a microbicide becomes available.
- Researchers and activists need to provide evidence that will help make the case that microbicide products are safe and that the risk (e.g., potential for increasing risk behaviours) to benefit ratio is justifiable. This will be especially important if a low efficacy microbicide is seeking approval for availability to the general public.
- Engage staff members of the various regulatory agencies in Health Canada and Industry Canada in microbicides dialogues and meetings to build their readiness to address regulatory issues for microbicides and expedite its approval processes.

When we're involved in the discussions on microbicides, it acts as training, brings us up to speed on the issues and the language. Then [Health Canada] can help expedite the process in the long run. We haven't been invited to the Microbicides Symposia in the past but I think it'd be helpful if we were there. (Interview #18)

¹⁵³ The Case for Microbicides: A Global Priority WHO Fact Sheet No 242 *Women and HIV/AIDS*, June 2000.
<<http://www.who.int>>

¹⁵⁴ Microbicide Watch: An Update and Analysis of Microbicide Research and Development.

- Canada can provide model regulatory systems to developing countries so that they are able to regulate the microbicide products on their own without relying on the US's FDA for approval and regulation.
2. Coordination of Manufacturing, Production and Regulatory Issues
 - Canada needs to develop a central secretariat body (something akin to the Alliance for Microbicide Development) which would track research and development efforts globally and domestically and institute the regulatory structures needed to expediently make microbicides available.
 - Regulatory agencies and funders should collaborate in discussing public policy issues around intellectual property, access and regulatory mechanisms, including issues such as inappropriate use of microbicides, and minimizing risks of driving selection of drug-resistant variants with ARV-based microbicides.
 3. Explore Innovative Purchasing Systems
 - Equity pricing, financing and bulk procurement for ARVs for developing countries will pave the way for access to vaccines and microbicides. One program that could serve as a model is CIDA's purchase of Vitamin A for distribution through UNICEF to developing countries.
 4. Post-Approval Surveillance
 - Microbicides regulators should also establish policies, guidelines and structures for post-approval surveillance, including reliable and ethical registries.

4. Access and Delivery

Promoting Informed Choice

Microbicides must be promoted and provided within the context of informed choice for a range of options that support individuals' sexual and reproductive rights. In several international conventions and conference programs of action¹⁵⁵, the international community affirmed that individuals must have the right to make decisions regarding their sexual and reproductive health, free of discrimination, coercion and violence. Efforts to provide access to microbicides must include work to remove barriers to informed choice as a result of social factors, laws, policies, service-delivery practices, resource constraints and service providers' attitudes. Thus, promotion of informed choice must include ensuring availability, access and use at three levels: individual/community; service delivery; and policies.

Ensuring Availability, Access, and Use

Promoting action to plan for availability and accessibility—in particular, policy dialogue with decision makers—needs to happen well in advance of a product being proven effective. The acute need for microbicides in many developing countries makes it critical to take action now to identify and address constraints to availability and access. Many of these constraints, such as problems of cost, supply, logistics, distribution, quality assurance, and consumer information, echo experience with development and introduction of other drugs and technologies. Depending on the active ingredient, some microbicides may be restricted to prescription only until there is sufficient experience of use in the general population. However, devising ways to improve access by making microbicides available over the counter from the outset is essential if they are to have a significant impact on the HIV/AIDS epidemic.

Ensuring access will include establishing and engaging innovative distribution networks, as well as traditional health service delivery points, pharmacies, and retail outlets. These products will also need to be made available at an affordable price, or in some cases, at no charge. International agencies and governments need to devise funding and distribution mechanisms to facilitate government procurement and subsidies. Pricing may also be influenced by taxes and tariffs on imported pharmaceutical products. This challenge could be addressed, in part, by building local manufacturing capacity, but the level of investment required and companies' willingness to invest require further examination. Effective education strategies will be essential to ensure that both the public and individual consumers understand the concept and potential benefits of microbicides, their risks and limitations, particularly if a product is only partially effective, and their proper use. Regardless of the distribution channels, health professionals are likely to be important opinion leaders and must also be targeted for training and education about microbicides. There is considerable scope to learn from experience with existing prevention methods, other nonprescription products, and social marketing approaches. In addition, a growing body of research is beginning to examine ways to convey appropriate messages specifically about microbicides and their use.¹⁵⁶

¹⁵⁵ Examples include the International Conference on Population and Development (Cairo, 1994) and the Fourth World Conference on Women (Beijing, 1995)

¹⁵⁶ The Case for Microbicides: A Global Priority WHO Fact Sheet No 242 *Women and HIV/AIDS*, June 2000.
<<http://www.who.int>>

Although it is hoped that one or more of the potential microbicides will have a positive risk–benefit ratio, they may have only partial efficacy, perhaps being as low as 35% effective. Indeed, the effect of these agents may be even lower when they are used outside of a clinical trial. Alternative approaches that require less attention and action from users—such as vaginal rings, more potent, longer acting products, or combinations of agents that might need to be used only once a day—could increase the effectiveness of microbicides and therefore have a much greater effect on HIV transmission.¹⁵⁷

Affordability

Although there is strong consensus that microbicides should have nominal or no cost in the developing world, there is lower consensus on how microbicides should be priced in developed countries. There are certain populations in Canada that are marginalized by economic ability to pay for the drugs on their own and should be able to receive microbicides free of charge (or for very minimal cost), such as through drug formularies for Aboriginal people. However, in order for pharmaceutical companies to have adequate incentive to invest in microbicide development, they will have to be able to make profits in the markets of rich industrialized countries. Microbicides could be provided to Aboriginal people free of charge, for example, through the First Nations Inuit Health Branch drug formulary, but this would compromise the ease of access of microbicides since individuals would need a prescription to access the microbicide this way.

Each provincial or territorial health jurisdiction will determine policy details around age eligibility, availability by prescription, over the counter or behind the counter of pharmacies. The federal government (Health Canada) could make recommendations for distribution of microbicides, co-funding early distribution initiatives, and providing microbicides in international development projects.¹⁵⁸

We also have a very good public health system where we are used to dealing with new products and making them universally accessible - people aren't denied health care. If this was to be a prescription drug, most people have some sort of provincial health plan that covers their prescriptions. If it's not a prescription, there will be policies needed around affordability. (Interview #14)

Acceptability

Social research is needed to improve understanding about the determinants of product use and user effectiveness and to evaluate acceptability in parallel with product development. Existing acceptability studies indicate that multiple formulations are needed to meet women's different needs and preferences. Ongoing research related to product formulation and mode of delivery should be expanded to ensure the best chance of developing a successful product. In anticipation of product introduction, research about how women and couples understand, negotiate, and act on information regarding partial effectiveness and a hierarchy of prevention choices needs to be expanded.

¹⁵⁷ Jonathan Weber, Kamal Desai, Janet Darbyshire, on behalf of the Microbicides Development Programme. The Development of Vaginal Microbicides for the Prevention of HIV Transmission... PLOS Medicine. May 31, 2005.

<<http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0020142&ct=1>>

¹⁵⁸ Information from Interview #6.

We could participate in pilot studies of delivery to marginalized populations (sex workers, street youth, IDUs, Aboriginals) once there is a product, developing delivery guidelines and evaluating the use of microbicides. Even before that, we should do studies in populations to determine acceptability, uptake and critical factors, and make policies regarding age, over-the-counter or prescription, those kinds of issues. (Interview #6)

Accessibility

A major social research question that will need to be addressed is that of affordability of microbicides, once they become available. It is essential that microbicides get into the hands of women and men who need it at a price they can afford. In the past, new health technologies usually do not become widely available in developing countries until more than a decade after their approval in the US and Europe, an unacceptable delay for life-saving technology developed primarily with public funds¹⁵⁹. Advocates are working with researchers and policy makers to emphasize the need to address issues of access and affordability up front, in order to be prepared to rapidly deliver a microbicide as soon as one is proven safe and effective.

We need to understand how we're going to approach people for trials, in a way that will make ordinary women and girls feel that this is a product for them. We'll have to look at Issues of delivery, access, treatment literacy, attitudes, health belief models, how to make innovation diffuse in a way that doesn't defuse interest. (Interview #13)

Assuming we have a safe and effective product, social research will inform how best to ensure that microbicides are used in specific communities such as gay men, Aboriginal women, or sex workers. One specific issue that needs to be explored is how best to license microbicides so that they are affordable to the largest numbers of people both in Canada and internationally. Once microbicide products are ready for distribution and given the likelihood of partial efficacy, social research needs to inform which sub-populations should be targeted for promotion of microbicides, and to work through issues of acceptability, packaging, pricing, and coverage through drug formularies. One issue in Canada that needs to be addressed is whether or not microbicides should be listed on drug formularies so that they are provided free of charge to vulnerable populations, such as Aboriginal people, or if they should be sold in pharmacies (e.g., over-the-counter as with emergency contraception).

Learning Lessons from Other Reproductive Health Technologies

From a human rights aspect, women have a right to access contraceptive choices, and there should not be any hurdles preventing their access to drugs or therapies that are proven to be safe and reliable. There are some important lessons to be learned from Canada's experience in having emergency contraception ("the morning after pill") deregulated as a prescription drug and listed on Schedule 2, i.e., accessible behind the counter of pharmacies. Women's reproductive rights organizations are currently working to have emergency contraception given unscheduled status (i.e., on the shelves of pharmacies). One argument against de-listing emergency contraception was the concern that women wouldn't be able to properly read the instructions and use the emergency contraception properly, but studies have proven that women are very capable of understanding the directions. The instructions are clear and simple, there are clear warnings regarding certain allergies, and no medical intervention is required to administer the emergency contraception. Emergency contraception is time-sensitive; in many cases it is impractical for women to obtain a prescription

¹⁵⁹ Fact Sheet #2: Frequently Asked Questions About Microbicides. <[http://www.global-campaign.org/clientfiles/FS2-FAQs\[E\]07.pdf](http://www.global-campaign.org/clientfiles/FS2-FAQs[E]07.pdf)>

from a doctor within the necessary 36 hours. The situation would be the same with microbicides for all of these factors. Women's reproductive rights organizations have been working since the late 1990s to make these policy changes for emergency contraception and are thus very experienced in long-term advocacy on issues such as microbicides.

Lessons have also been learned through efforts to distribute and market female condoms. In some developing countries, women perceive the female condoms as prevention technology for sex workers, and not for "regular people." Lessons will also be learned through the rollout of the *Gardasil*TM vaccine for human papilloma virus, which was recently approved for use in Canada.

Anything to do with sex raises all kinds of barriers. It would be interesting to understand the arguments against making emergency contraception available – that it would increase promiscuity, for example. There might be similar arguments with microbicides. (Interview #3)

Areas for Action

1. Prioritize Access

When the first microbicide products are available, governments will have to prioritize which populations should have priority for access to the microbicides, especially in light of the fact that the first products will have partial efficacy.

2. Ensure Supportive Policy Framework

- Ensure that purchasing agreements between health jurisdictions and manufacturers are established in advance of microbicides being available on the market. In Canada, the federal, provincial and territorial health departments must establish purchasing agreements, and at a global level, CIDA, the WHO, UNFPA and GFATM may hold such agreements.
- Provide information to convince policymakers, in developed and developing countries, about the potential role of microbicides in preventing HIV and other STIs. This will include analysis of the potential cost-effectiveness and public health impact of microbicides with a range of characteristics, in a range of settings, and in comparison and combination with other preventive interventions.
- Promote dialogue with decision makers in developing countries and provide technical support to prepare national policy frameworks for microbicides introduction, promotion, and delivery, through health systems and as over the counter products.
- Consider potential strategies for promoting access and affordability—for example, advocacy with WHO or other competent approval agencies to ensure microbicides are included in Essential Drugs Lists, bulk procurement, subsidies, incentives, and the potential of different financing mechanisms.
- Policies should also be developed to ensure that consumers have access to microbicides through access points that are non-judgmental and don't impose unnecessary barriers. Barriers facing certain populations should be removed, such as barriers faced by immigrant or refugee women in accessing medical and health information due to language barriers and power imbalances in health care relationships.

One policy issue is the difficulty of young people to access certain sexual and reproductive health resources, due to power of health care and pharmacy professions. In spite of the fact that any young person is supposed to be able to access any health product, we know that there are a lot of barriers – parental permission, artificial age limits, pharmacists who “don’t believe in it” and thus won’t sell emergency contraception. Because the rights of young people are not being upheld, there are policy implications. (Interview #3)

3. Ensure Broad Distribution Systems and Access Points

- Increase the involvement of international, bilateral, and technical agencies that could contribute to microbicide availability, access, and affordability, based on their areas of comparative advantage—for example, UNAIDS through its global leadership on HIV/AIDS, UNFPA through its mandate to support provision of essential reproductive health commodities, the World Bank through supporting pricing and financing mechanisms, and UNICEF through its focus on women and children and expertise in communication, community mobilisation, and product procurement and distribution.
- Build on the Global Campaign for Microbicides, involving a wider range of organizations in developing and developed countries in strategies to ensure microbicide availability and access—for example, social marketing organizations, women’s groups, organizations working on HIV/AIDS and on sexual and reproductive health, development agencies, community organizations, and the media.
- Build on existing models of procurement and distribution of condoms and bed nets in developing countries. The Global Alliance for Vaccines and Immunization provides some transferable models of immunization distribution. Organizations such as Population Services International, an NGO promoting greater access to health care and services, HealthBridge (formerly PATH Canada) in distributing and providing training on insecticide-treated bed nets, and Family Health International which has conducted extensive social marketing on condoms and acceptability research on emergency contraception, are key international partners to engage in microbicides distribution and promotion.

In smaller rural communities where points of accessing products are limited, there has to be easy access, and getting acceptance in the communities would be important. In the large centres, there are lots of organizations that could be actively involved, but the challenge will be in small rural or marginalized areas. Access would be a big issue for Aboriginal communities. (Interview #3)

- Build readiness of access points that are most appropriate for reaching target populations, such as women's health clinics, sexual and reproductive health clinics, family planning clinics, supermarkets, bars, and community-based organizations working with these populations.

4. Scale up Distribution

Canada can help scale up delivery of microbicides through policies and programs which ensure that microbicides are affordable and widely available through a variety of service outlets. CIDA, for example, could create a policy that microbicides education, promotion and distribution is included in all HIV and STI programs.

- Canada can also develop policies that can serve as sample legislation for countries on how to scale up access of microbicides.

5. Ensuring Affordability

- The Canadian government should implement regulatory options to ensure the affordability of products for the prevention and treatment of HIV/AIDS.
- Canada should exercise its right as a WTO member to make full use of the safeguard provisions of the TRIPS Agreement in order to protect public health and promote access to medicines.

6. Education

- A comprehensive education strategy must be developed by all stakeholders and be adequately funded in advance of, during, and after microbicides become available on the market.
- Peer education programs should be supported (e.g., amongst young women) and ensure that microbicides information is available through sexual health education in schools, through community-based organizations and through public health services.
- Messages should incorporate microbicides as one tool in the prevention continuum, continuing to promote condoms and other prevention methods. Lessons should be taken from the harm reduction approach to education, framing microbicides as only one tool in the spectrum of prevention tools and strategies.
- Develop appropriate strategies for product promotion, delivery, and marketing, and for educating health professionals and potential consumers. Explore the best ways to promote microbicides in the context of other prevention options and without undermining condom use. Conduct further behavioural research to improve understanding of protective behaviour in relationships, product preferences, and acceptability of microbicides to women and men.

There are some lessons to be learned from the HPV vaccine – there was lack of education, it was left a little bit too late, not up-front enough. We can't wait to educate people until after licensure gets through in the US, and then provide messages in Canada, we shouldn't be reactive. The problem with letting the US come out first with their messages is that they have their own set of controversies. They want to couch it as prevention of cervical cancer, rather than prevention of an STI. We need to have our education and information ready to roll at the same time as the Americans, and we need an approval process at same time as the US. We also need education strategy early and upfront. (Interview #19)

7. Develop Appropriate Marketing Messages

With support from private and public funders, community-based organizations should work to develop microbicides marketing messages that address the realities of access and their use, taking into account a variety of considerations such as:

- expressing that “microbicides are for the world” and will be of value for HIV prevention both in communities in Canada and in developing countries.
- targeting populations and culturally-appropriate messaging and access points for women, youth and gay men, and for Aboriginal people, African or Caribbean Canadians, prisoners, people who use injection drugs, sex trade workers, people living with HIV, and street youth.
- viewing microbicides as only one tool in the prevention continuum and providing another “informed option” along with condoms.
- discussing contexts of microbicide use – such as with casual or primary partners, with or without the partner being aware.

- explaining the purpose of microbicides among various users – such as for HIV prevention, STI prevention and/or contraception.
- outlining the most recent developments in microbicides research and clinical trials.
- taking into account language and socioeconomic differences.

8. Optimize Usability

Canadian researchers and producers should seek microbicide products that recognize the need for a truly woman-controlled prevention tool. Microbicides should meet usability standards to ensure that women and men will use them, such as not having any taste or detectable texture, being able to be applied covertly, lasting for a prolonged period of time in a variety of storage conditions, being affordable, and being able to be applied regularly without irritation.

The main advantage of a microbicide would be if it could be used covertly. It must be user friendly for women for it to be truly female controlled, and should not be able to be controlled by men in terms of dictating its use. There are lessons to be learned from female condoms – which was not truly a woman's decision. For example, there needs to be a way for a sex worker to use microbicides without the john noticing her applying it or the feeling of it. (Interview #8)

5. Community Education, Mobilization and Engagement

Canada's Strength in Community Engagement

Canadian civil society is generally very active in HIV/AIDS advocacy, policy development and program delivery. Canada's community-based HIV/AIDS organizations serve a very wide range of communities and are seen to be leaders in meaningful involvement of communities. Canada's model of community engagement can set a global example and demonstrate the importance and value of involving people who are affected as early in the microbicide development process as possible so that they can have an impact in shaping the distribution and access of a microbicide.

Canadian civil society also has an important and significant role to play in collaboration with researchers, especially clinical and social researchers. Since the 1990s, community-based research in the HIV/AIDS field has gained profile and legitimacy. "Community-based research" refers to research processes which are, to various degrees, driven by, or responsive to, the needs and interests of a specific community. Community-based research is a form of research in which principles of community involvement and collaboration are applied using scientifically accepted research methods. The research must demonstrate direct community involvement, community relevance, equity in partnerships and methodological rigour.¹⁶⁰

Community partners, clinicians and social workers can inform and guide researchers and policy makers about target communities with respect to perceptions of health and risk, gender implications, and effective outreach and messaging strategies. Continuous feedback loops of communication and information must be maintained between researchers and community partners. Community partners need updated and accurate information about microbicides R&D in order to develop effective communication plans, and researchers need to be aware of community perceptions and trends as they evolve in order to conduct their research.

MAG-Net

Since 2000, CAS has coordinated the activities of the Microbicides Advocacy Group Network (MAG-Net). MAG-Net is a coalition of Canadian ASOs, international development NGOs and other community-based organizations interested in promoting the development of new HIV and STI prevention options. MAG-Net is coordinated by CAS and serves as the Canadian partner of the Global Campaign for Microbicides.

Global Campaign for Microbicides

Internationally, the GCM is a broad-based, international coalition of community groups and advocates, working to build support among policymakers, opinion leaders, and the general public for increased investment into microbicides and other user-controlled HIV/STI prevention methods. Through advocacy, policy analysis, and social science research, the GCM works to accelerate product development, facilitate widespread access and use, and protect the needs and interests of users, especially women.

¹⁶⁰ Canadian Institutes for Health Research. HIV/AIDS Community-Based Research Program. <<http://www.cihr-irsc.gc.ca/e/25182.html>>

International Rectal Microbicide Advocates

Convened by the AIDS Foundation of Chicago, CAS, the Community HIV/AIDS Mobilization Project and the GCM in the spring of 2005, IRMA is currently a network numbering (as of November 2007) over 500 advocates, policymakers and leading scientists from 38 countries on five continents working to advance a robust rectal microbicide research and development agenda. IRMA hosts a moderated listserv and sponsors regular international conference calls featuring presentations on the latest in rectal microbicide research. IRMA's objectives are:

- To advocate for accelerated research, development and access to safe and effective rectal microbicides.
- To promote rectal safety studies on all viable vaginal candidate microbicides.
- To demand safety data on sexual lubricants currently on the market.
- To support, where appropriate, the research of other new prevention technologies, such as vaccines and oral prevention (PrEP), and to promote existing prevention methods such as male and female condoms as part of a range of prevention options.
- To serve as a central forum for exchange, debate, networking on rectal microbicides.
- To convene diverse perspectives and scientific disciplines to improve understanding and action.

The history of the microbicide movement is based in the obvious gap in female-controlled prevention tools. The microbicides movement hasn't had much success until recently in grappling with how to engage other constituencies without losing focus on women, how to be inclusive without being exclusive. So now we have the Rectal Microbicides groups - in the UK, USA, Canada, Nigeria. There's now a listserv with 75 members in 8 countries around the world. We're now developing a paper on rectal use of microbicides, and the focus is making sure that we're not putting out messages that people interpret as they're not getting their fair share in relation to vaginal microbicides. (Interview #15)

Alliance for Microbicide Development

The Alliance for Microbicide Development is a global, non-profit organization whose sole mission is to speed the development of safe, effective, and affordable microbicides to prevent sexually transmitted infections, most critically HIV/AIDS. The Alliance was founded in 1998 as an agent of change at a time when progress in microbicide research was slow, fragmented, and severely underfunded. A coalition of representatives from over 200 biopharmaceutical companies, nonprofit research institutions, and health advocacy groups, the Alliance catalyzes support for its mission through advocacy, education, monitoring, research, trouble-shooting, convening dialogue around key issues, participating in dynamic and committed partnerships, and networking across constituencies, disciplines, and sectors.

African Microbicide Action Group

The African Microbicides Advocacy Group (AMAG) is a coalition of microbicides advocates from organizations and institutions based and/or working in various African countries. AMAG was launched at the 2004 International Microbicides Conference. The AMAG network has over 250 members from 28 countries across Africa and beyond. Members are community advocates, researchers, scientists, policy makers, media and service providers - working in HIV care, treatment, advocacy, research, information-management; gender equality, sexual and reproductive health/rights; poverty and economic development, and human rights. Members represent diverse communities, groups and cultures within the Africa Region, but share a commitment to supporting the process of developing a microbicide that is ethically developed, effective, safe and accessible. They take a human rights-based approach that promotes the rights of all people to equitable access

to HIV/AIDS prevention, treatment, care and support. The main aims of AMAG are to ensure that a coordinated African voice is engaged in setting and moving forward the microbicides advocacy agenda in Africa and internationally, and to support participating organizations to prepare for more effective, better coordinated microbicide advocacy in their own contexts and between African countries.

Role of Community-Based Organizations in Accelerating Microbicide Development

Community involvement is crucial in generating funding, raising awareness and putting microbicides on the political agenda. Raising microbicides awareness, particularly among vulnerable populations, will prepare communities for participation in trials, and will ensure effective microbicides delivery and use. Given that public sector support is required to fund microbicide research, it is important for the governments to understand and communicate that all Canadians will benefit significantly from the availability of microbicides.

Therefore community-based organizations can:

- Raise awareness about microbicides in communities.
- Make politicians and government policy makers aware that Canadians need access to microbicides as soon as possible and at a reasonable cost.
- Make the media aware of microbicides and their importance to Canadian communities.

Specifically, community-based organizations can become involved in raising awareness on microbicides by:

- Distributing microbicides information to their membership through newsletters, action alerts, journal articles, or e-mail list serves.
- Including information about microbicides in their organizations' education and advocacy activities.
- Planning a workshop or session on microbicides at meetings or conferences.
- Posting information on websites.
- Sending an op-ed piece or a press release regarding microbicides to local media.
- Organizing a showing of the Global Campaign for Microbicides' video *In Women's Hands* or organizing a showing of the *Giving Women Power over AIDS* exhibit on microbicides.

Advocates should work together to support¹⁶¹:

- Development of National HIV/AIDS Plans or Strategies that adopt a human rights framework promote the prevention–care–treatment continuum and include a comprehensive approach to HIV encompassing treatments, microbicides and vaccines as well as voluntary counseling and testing, education, harm reduction, condom distribution, care and support, and efforts to address stigma, discrimination and gender vulnerability.
- Development of minimum standards against which advocates can hold Southern governments to account for national budgetary allocations to HIV treatment and prevention, research efforts and the strengthening of health delivery systems.
- Promotion of the involvement of people living with HIV/AIDS and civil society groups in the development, content, implementation and monitoring of national plans.

¹⁶¹ Canadian HIV/AIDS Legal Network (2004). HIV Treatments, Microbicides and Vaccines: Developing an agenda for action — Background Paper. <<http://www.aidslaw.ca/publications/publicationsdocEN.php?ref=360>>

- Development of checklists of essential items relating to R&D and access as an evaluation and accountability tool for assessing National Plans (e.g., community involvement, ethical review, regulatory issues).

"We have a really strong community-based movement that has been involved in microbicides for the last 6 years, longer than most countries. We've managed to achieve a lot - if you ask the Global Campaign for a comparison with other countries, they'll tell you that Canada is one of the most organized and most active advocacy networks with many partners. In terms of advocacy, getting the Canadian government to make a contribution to the IPM, doing national multi-stakeholder Symposia, leading to this Action Plan - no other country has done this. We've done really well and it's a strength that we can build on. The whole multi-sectoral approach is a really strong base and fairly good history in HIV/AIDS work in general, like with Leading Together, the Federal Initiative, the HIV Vaccines Plan. And we have real strengths in community-based research to inform what we need to do domestically and internationally." (Interview #15)

Areas for Action

1. Develop a Communications Strategy

Develop a communications strategy around the CMAP that would press specific issues and would include the messages of:

- microbicides as part of broader prevention strategies, and as part of the continuum of prevention, diagnosis, care, treatment, and support.
- the need for resources to support microbicides research and development.
- planning for accessibility and delivery of microbicides.
- framing microbicides as being compatible within the Canadian movement to integrate HIV and STI initiatives.

A lot of education will have to happen once a product becomes available. The first generations of microbicides will have low efficacy and people will have to be very clear about the decisions that they are making and understand the risks. We will see a decrease in HIV transmission across populations, but there will still be infections at individual level despite using a microbicide. These are complex messages. And we will have to educate about the different uses of microbicides - vaginal microbicides might not only be ineffective rectally but could also be harsh and cytotoxic. (Interview #29)

The strategy would engage multiple stakeholders, including HIV/AIDS, development, and the sexual and reproductive health communities, and would include a population specific social marketing plan.

2. Develop Partnerships

- Community-Based ASOs, in collaboration with women's groups and organizations, should enhance their microbicides advocacy efforts by building on the experience in the women's sexual health and reproductive rights movement.
- Canadian community-based ASOs should be supported by policy makers, funders and leaders in vulnerable communities, to lead advocacy and awareness raising activities.
- Canadian community-based ASOs should encourage people living with HIV/AIDS to get involved in microbicides advocacy.
- Greater cross-sectoral engagement in microbicides advocacy and awareness raising is needed with organizations such as the Society of Obstetricians and Gynecologists of Canada, the

Canadian Pharmacists Association, the Canadian Women's Health Network, national Aboriginal organizations, Status of Women Canada, and gay/lesbian/bisexual organizations.

- Canada's twinning projects should focus on microbicides, transferring lessons between domestic and global partners to mobilize as rapidly as possible relevant education, develop appropriate messages, and strategize how to do the roll-out.

Health advocacy groups need to be more involved, and we need to continue to draw on southern voices who support microbicides research so it's not just seen as being driven by the north. (Interview #8)

3. Raise Awareness Amongst Vulnerable Communities

Canadian community-based organizations working in HIV/AIDS, in women's health and social issues, with Aboriginal communities, with youth, with sex trade workers and with prisoners, should:

- integrate microbicides advocacy, education and promotion into their other ongoing safer sex messages. An awareness campaign designed specifically for young people will be helpful in motivating youth to get involved in microbicides advocacy.
- continue to raise awareness about microbicides and their potential benefits for all men, particularly gay men and MSM, encouraging them to participate in research and advocacy efforts for the development of vaginal and rectal microbicides.
- raise microbicides awareness among Aboriginal people, newcomers to Canada and among members of various ethnocultural communities. Information about microbicides should be culturally appropriate and included in all safer sex messages. In particular, women from these communities should be targeted for awareness-raising and mobilization efforts, as the urgent needs and specific circumstances in these communities requires effective microbicides activism, and strong efforts to prepare these communities for microbicides use once they become available. Messages should focus on microbicides as a possible HIV/STI prevention tool and prepare communities for eventual microbicides delivery.
- ensure that persons who use drugs, including those who inject drugs, are aware of the potential benefits of microbicides and are actively involved in microbicides advocacy. Microbicides awareness should become part of the safer sex messages for all persons who use drugs.
- include information on microbicides in their prevention messages to prisoners and prison officials. In collaboration with prisoners rights advocates, ASOs should advocate with prisoners for policies and procedures that would ensure speedy access to microbicides for prisoners once they become available.

4. Advocate for Increased Funding

- Community advocacy that demonstrates a strong need and urgent demand for these products can play a crucial role in mobilizing needed resources.
- Communities need to apply sustained lobbying pressure for low-cost and convenient access to microbicides for the poor, both domestically and internationally.
- Funding for microbicides research and development must include support for grassroots community-based organizations at the local level, as well as for national and international NGOs, in order to develop multi-level expertise and preparedness for microbicides.

I think it is important that some modest funding extend down to grassroots organizations at the local level. Otherwise, the larger national and international NGOs develop an expertise that is disseminated outwards but falls on 'deaf' ears. You can have an ultramodern radio transmitter, but if the people at home are too poor to buy a radio, then news will not flow. (Interview #2)

5. Participate in Research

- Members of the community should understand and be actively involved in all aspects of the research process. This could involve identifying the research question, collecting and analyzing data to reporting and applying the results. In short, the community has a multi-dimensional role to play in research: it should be an advisor, collaborator and partner.¹⁶²

6. Raise Public Awareness

- Initial education for the general public is necessary to “prime” them for the concept of microbicides and provide them with basic information necessary to distinguish between legitimate and ineffective products.
- In Canada, where few clinical trials are likely to take place, community involvement can focus on raising awareness, advocacy and planning for shifts in prevention programs and policies as a result of the impact of the introduction of microbicides.
- Community education can help alleviate possible effects of unfounded microbicide optimism resulting from clinical trials. Key messages should emphasize that microbicides are not yet available, and that when they are, they should be understood as an additional tool that is complimentary to existing prevention methods. Together with researchers, community members can help to avert unfounded optimism by emphasizing prevention. Public awareness can also help to generate demand for microbicides, playing a role in mobilizing financial resources and can help to prepare communities for delivery and use of microbicides when they become available.

7. Facilitate Clinical Trials

- Community members, through CBOs and NGOs, should play an active role in investigating ethical standards of clinical trials and collaborate with researchers in keeping communities informed of the latest developments in microbicides research.
- Vulnerable communities should be well represented in any clinical trial. Women from all parts of society should have access to trials, including young women, and women from Aboriginal communities and women of African or African Caribbean descent. Potential microbicides should also be tested for rectal use, and safety of oral exposure, in both men and women.
- Work with researchers to ensure that ongoing processes of informed consent are being implemented.
- Communities can engage in educating their members about microbicides and related trials, and work towards reducing HIV-related stigma and discrimination.¹⁶³

¹⁶² “Community Involvement in Microbicide Trials: A Dialogue”, Dialogue in Southern Africa: Global Campaign for Microbicides, Washington, 2004.

¹⁶³ See Guideline 2, UNAIDS, “Ethical Considerations in HIV Preventive Vaccine Research”, UNAIDS Guidance Document, 2000.

8. Lead Rectal Microbicides Advocacy

IRMA has been actively engaged in raising the profile of rectal microbicides globally. IRMA continues to pursue a number of key activities to which Canadian advocates can contribute, including:

- Advocating strategically for more resources and more research into rectal microbicides.
- Advocating to ensure all current and future vaginal microbicides products are tested for rectal safety and effectiveness.
- Advocating for more research into the rectal safety of lubricants.
- Constituency-building with gay communities, women, PHAs and communities from developing countries to strategize about the relationship of rectal microbicides advocacy to general microbicides advocacy, gay men's health, women's health, etc.
- Resource development, including web-based materials, fact sheets, presentations, etc.

9. Support Community Involvement

- Given that lack of resources is the main constraint for community-based organizations to get more involved in microbicides advocacy and awareness raising, there should be funding available for organizations to dedicate staff time and organizational resources to this work.

Community will be very important. Women in villages must understand what it is and how to use it. They won't use it until they understand, so we should be working with local health workers, community-owned resource persons, community-level expertise to help people understand benefits and how to use them. Canadian organizations would support through resources to do that work. (Interview #10)

6. Gender Analysis

We fully recognize that the goal is to move toward a time when everyone has the power to make his/her own decision about sexual safety. In the meantime, there are hundreds of cultural changes that will help us get towards sexual empowerment. Microbicides are one more tool that will help women get towards having the ability to fully negotiate their sexual rights. Not providing the tool is not going to help women get any closer to that end goal. Case example: a woman is finally able to get free after going through a very long struggle to get out of an abusive situation, but because she didn't have the means to protect herself in the meantime, she found out that she was HIV-positive. It's hard for people to think about a risk that they can't do anything about...that's why many women just don't want to think about HIV because there's nothing they can do to protect themselves, and it leads them to deny risk. Providing a tool will empower women to take care of themselves, to protect themselves in that one regard. Empowerment builds empowerment. (Interview #31)

Why a Gender Analysis?

An overview of HIV/AIDS rates and issues specific to men and women is provided in the section on “Population-Specific Issues” (page 21 above). This section of the CMAP aims to go beyond a description of the differences in HIV vulnerability between men and women, and provides a gender analysis of the importance of microbicides. Adopting a gender perspective is now generally considered as the most effective way to address the HIV/AIDS pandemic. Gender roles and relations powerfully influence the course and impact of the HIV/AIDS epidemic. Gender-related factors shape the extent to which men, women, boys and girls are vulnerable to HIV infection, the ways in which AIDS affects them, and the kinds of responses that are feasible in different communities and societies.¹⁶⁴

Gender dynamics are understood as the different roles, expectations, identities, needs, opportunities and obstacles that society assigns to women and men based on sex. Girls and boys, women and men, have the same rights, potential and capacities; but discrimination against girls and women based on socio-cultural norms often relegates them to lower status and value. This often places them at considerable disadvantages in terms of their access to resources and goods, decision-making power, choices, and opportunities across all spheres of life. While sex is biological, gender is socially-ascribed. It determines how individuals and society perceive what it means to be male or female, influencing one's roles, attitudes, behaviours and relationships - aspects of personal identity that have a direct bearing in sexual decision-making and the HIV/AIDS pandemic.¹⁶⁵

International commitments¹⁶⁶ have affirmed the need to explicitly address the gender-based inequities and ramifications of the pandemic. Though complex and challenging, gender mainstreaming across the broad range of responses to HIV/AIDS is necessary to halt the epidemic.

If a company took a strong microbicide product, they'd make a fortune - because women are more reasonable than men, around the world. I'm convinced of that. But we need to protect women because they don't control their sexual destiny - they have great difficulty telling a man to wear the condom in heterosexual relations. They are more reasonable when it comes to sex, for self-protection and for their children. It's a big problem in sexual relations - power by men over women. (Interview #20)

¹⁶⁴ UNAIDS (2001). Fact Sheet: Gender and HIV/AIDS. http://www.unaids.org/fact_sheets/ungass/html/FSgender_en.htm

¹⁶⁵ UNFPA: HIV Prevention Now, *Programme Briefs* No.4 - Addressing Gender Perspectives in HIV Prevention - February 2002. <<http://www.unfpa.org/hiv/prevention/documents/hivprev4.pdf>>

¹⁶⁶ The ICPD Programme of Action (8.28, 8.29a). The 1995 Beijing Conference Platform of Action (para.108). The ICPD and Beijing five-year reviews. The UN General Assembly Special Session on HIV/AIDS (UNGASS 2001)

Women's Need for Microbicides

HIV cases among women in Canada are rising. In 2006, women constituted more than one quarter of all new HIV cases.¹⁶⁷ Amongst these women, HIV rates are highest among Canadian women aged 15 to 29 years. In 2003/04, this group accounted for 42.5% of HIV-positive reports among women.¹⁶⁸ At the same time, older women in Canada (aged 40 to 49 years) are increasingly at risk of contracting HIV. Women of this age group constituted 23% of HIV reports in adult females by 2002.¹⁶⁹ According to Health Canada, heterosexual contact and intravenous drug use are the main causes of HIV transmission in women.

Because of female biology, women are at greater risk of contracting HIV through unprotected heterosexual sex because HIV is transmitted eight times more efficiently from men to women, than from women to men. Women have a much larger area of skin and tissue that is exposed to their partner's secretions during sex than men. Additionally, HIV-infected semen has a higher concentration of the virus than vaginal secretions.

Women also often have limited control over safer sex decisions as women can be socially and/or economically dependent on partners, limiting their power to negotiate condom use. A microbicide that is odourless and tasteless will be especially beneficial to women as they will be able to take more control over protecting themselves. In addition, many products currently in trials could provide protection against STIs. Not only will microbicides prevent HIV or STI re-infection, but also the benefits of microbicides will be bi-directional; protecting both partners and some microbicides will also have contraceptive properties. Microbicides may also provide an option of skin-to-skin intimacy and may be pleasure enhancing.

Women who have sex with women may also benefit from future microbicides. Though more research is needed to understand HIV transmission among lesbian women, there is the potential of STI transmission between lesbian women through shared sex toys and having an STI has been shown to increase the risk of contracting HIV.

I have been interested in STIs for more than 30 years, in 1992-93, I started to think about microbicides, even though the term didn't exist. I wanted to offer protection to women against STIs because they are more susceptible because of their anatomy. And the complications are much greater in women. For example, with gonorrhea women have major complications and become sterile. Generally, women are more susceptible to STIs (8:1 chances of getting STIs from a man that is carrying the microbes, versus a man exposed to a positive woman). Women carry children and can pass STIs to their infants. It's a silent issue amongst women, and often the complications are detected too late. (Interview #20)

Microbicides would provide a much needed woman-controlled method of HIV prevention. As the HIV epidemic progresses, women and girls are increasingly affected. At the end of 2005, women accounted for nearly half the 40.3 million people living with HIV around the world. In sub-Saharan Africa, 57% of HIV-positive adults are women. When combined with the persistence of gender inequality, economic disparities, and violence, females' increased biological risk further reduces

Declaration of Commitment on HIV/AIDS. Secretary-General's Report to the UNGASS, states "that gender inequalities fueling the epidemic must be explicitly addressed" (para.88).

¹⁶⁷ Public Health Agency of Canada. *HIV/AIDS Epi Updates*, August 2006, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2006: 5.

¹⁶⁸ Health Canada, *HIV/AIDS EPI Updates*, April 2003, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Health Canada, 2003: 2.

¹⁶⁹ Health Canada, *HIV/AIDS EPI Updates*, April 2003, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Health Canada, 2003: 2.

women's ability to protect themselves from HIV. Microbicides, which could be used with or without a partner's knowledge, would provide a prevention option for women that they could control.¹⁷⁰

Men's Need for Microbicides

Men accounted for 73% of new infections overall in Canada in 2006¹⁷¹ and men who have sex with men (MSM) accounted for 40% of new infections.¹⁷² In 2002, increased rates of new HIV cases were observed amongst other groups as well, including men who have sex with men (MSM) in some Canadian cities.¹⁷³ Gay men and MSM continue to account for the largest number of new infections in Canada. In 2002 they represented 58% of all PHAs.¹⁷⁴ This population also had the largest increase in infections, up 10% since 1999.

Microbicides will benefit men, including heterosexual men, gay men and men who have sex with men. Microbicides will provide bi-directional protection, protecting both partners during sex. There seems to be a widespread misconception that microbicides will not benefit heterosexual men or men who do not engage in anal intercourse. Men, like women, report low levels of condom use in long-term partnerships. Worldwide, men tend to have more sex partners than women, which often include extramarital partners.¹⁷⁵ The risk of contracting HIV thereby increases for them and their partners.¹⁷⁶ Secrecy and stigma may stifle discussion about HIV within couples.

Without men's commitment to microbicides and safer sex, successful HIV prevention is not feasible. This is especially true given that existing research suggests that women in many countries will not feel comfortable using microbicides without discussions with their male partner. Research conducted among men in the United States, Zimbabwe and Mexico revealed that Zimbabwean men were likely to demand that their female partners inform them if they were using a microbicide product. Mexican respondents stated if the microbicides acted as a contraceptive, it would be necessary for a woman to get her husband's consent. American men said that as long as a microbicide were safe, it would be the woman's decision whether or not to use it. Although some indicated that they would still appreciate their partners telling them.¹⁷⁷ Many men surveyed in all three countries emphasized the importance of microbicides safety. Efforts to promote microbicides and a women's right to sexual self-determination should go hand in hand.

The complexity of sexual decision making for some gay men highlights the need for more targeted information and other resources such as microbicides to practice safer sex. Recent Canadian data on

¹⁷⁰ By Betsy M. Finley and Carolyn J. Plescia (Winter 2005/2006). *The Future of HIV Prevention: New Tools, New Hope*. <<http://www.thebody.com/content/treat/art14134.html>>

¹⁷¹ Public Health Agency of Canada. *HIV/AIDS Epi Updates, August 2006*, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2006: 5.

¹⁷² Public Health Agency of Canada. *HIV and AIDS in Canada. Surveillance Report to December 31, 2006*. Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2007: 17.

¹⁷³ See, for example, L. Calzavara, E. Tharao, T. Myers. "Influence of immigration and country of origin on utilization of HIV-related services and programs: East African communities in Toronto," *Canadian Journal of Infectious Diseases*, 11 (Suppl. B) 2000: 64B.

¹⁷⁴ Health Canada, *HIV/AIDS EPI Updates*, April 2003, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Health Canada, 2003

¹⁷⁵ UNAIDS, *Men and AIDS - A Gendered Approach*, World AIDS Campaign, 2000, <<http://www.unaids.org>>.

¹⁷⁶ UNAIDS, *Men and AIDS - A Gendered Approach*, World AIDS Campaign, 2000, <<http://www.unaids.org>>.

¹⁷⁷ C. Coggins, K. Balnchard, B. Friedland, "Men's Attitudes towards a Potential Vaginal Microbicide in Zimbabwe, Mexico and the USA," *Reproductive Health Matters*, 8(15), May 2000: 136.

risk behaviors suggest that men who have sex with men continue to be at elevated risk of contracting HIV and other STIs by engaging in unprotected anal and oral intercourse with casual partners.¹⁷⁸ Among other factors, complacency towards HIV infection may have arisen because of lack of direct experience of the AIDS epidemic among younger gay and bisexual men, and a desire to escape a lifetime of rigorous safer sex.¹⁷⁹

The public debate over "bare backing"¹⁸⁰ amongst MSM highlights the fact that one tool (i.e., the male condom) for disease prevention is insufficient to effectively fight HIV. People protect themselves most effectively when they have a range of options from which to choose. Microbicides could thus offer an alternative to the current "condom versus no condom" decision. In addition, microbicides will allow skin-to-skin intimacy, thus enhancing pleasure. Microbicides, including products that have been tested for rectal use will be an important prevention option for all men to be used in combination with condoms.¹⁸¹

Microbicides as a User-Controlled Prevention Tool¹⁸²

Unlike the male or female condom, a microbicide could be used without gaining a partner's active cooperation at each act of intercourse, and therefore is conceptualized as a user-controlled, rather than partner-controlled, prevention tool. Social scientists have interviewed women in several countries to explore how they felt about the possibility of a user-controlled method. A large proportion of respondents said that if they planned to use a microbicide in the future, they would probably discuss the issue in advance with their husbands or boyfriends. But, they said, this could be a one-time conversation and would not have to be repeated each time the couple has sex.

Instead of interrupting passion, a male or female user could initiate the conversation in a neutral setting, simply as information sharing. Gaining the partner's passive agreement to the use of a microbicide in that context might well be easier than asking the partner to either put on a male condom or allow insertion of a female condom during sex. Thus microbicides could enable receptive sex partners to manage their own protection without the need to negotiate or interrupt sexual spontaneity every time.

The covert nature of microbicide use should be seen as a pragmatic benefit until we have the ideal world of totally open sexual relations, until that is a possibility. But microbicides are not a way to replace efforts to continue fighting for gender power balance in sexual relations. (Interview #9)

The thing that is appealing about microbicides is the difficulty of negotiating condom use – that's just a really difficult conversation for couples to have. That's the promise that they see in this technology. (Interview #2)

Some receptive sex partners, however, may choose to use a microbicide without any partner discussion. Although covert use of a microbicide will be especially relevant in situations of sexual

¹⁷⁸ Health Canada, *HIV/AIDS EPI Updates*, April 2003, Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Health Canada, 2003.

¹⁷⁹ M. Katz, "AIDS Epidemic in San Francisco Among Men Who Report Sex With Men: Successes and Challenges of HIV Prevention," *Journal of Acquired Immune Deficiency Syndromes Human Retrovirology*, 14, 1997, (Suppl 2) S38-46.

¹⁸⁰ D. Ostrow and D. McKirnan, "Prevention of Substance-Related High-Risk Sexual Behavior Among Gay Men: Critical Review of the Literature and Proposed Harm Reduction Approach," *Journal of Gay and Lesbian Medical Association*, 1(2), 1997: 97-110.

¹⁸⁰ "Barebacking" is a term usually used in reference to unprotected anal intercourse between men.

¹⁸¹ Canadian AIDS Society, *Community Mobilization Kit for Microbicides*, (2004).

<<http://www.cdnaids.ca/web/repguide.nsf/pages/cas-rep-0006>>

¹⁸² Global Campaign for Microbicides (2006). Fact Sheet #12: Microbicides Messaging: Themes to emphasize and avoid.

violence or coercion, it should be noted that the discovery of covert microbicide use may perpetuate violence. Initiating covert microbicide use in long-term partnerships could be somewhat challenging because several of the products now under development are likely to increase vaginal lubrication. Delivery systems are under development, however, that may minimize this effect. A flexible, microbicide-loaded vaginal ring, for example, offers the possibility of time-released protection with minimal lubrication change, thus meeting the needs of women who can't or don't want to discuss the issue of protection with their male partners.

Areas for Action

1) Conduct Social, Behavioural and Policy Research on Gender Issues with Microbicides

In general, research needs to be conducted alongside all other microbicides efforts to understand how exactly microbicides could change the underlying structures that disadvantage women with respect to HIV, STIs, reproductive health and gender-based violence. Targeted research funding opportunities should be provided to help develop a gender-based understanding of the differential impacts of microbicides for women and men including (but not limited to) the following topics:

- how best to ensure that users have access to microbicides in a variety of contexts and life situations.
- lessons learned with respect to differential access (e.g., as with ARVs) between men and women.
- impact of microbicides on issues of fertility, contraception.

When you have vaginal use of any substance - women automatically link this to birth control, and they think it will interfere with their reproductive abilities. So, we need to figure out if it will work both ways. (Interview #11)

- implications of microbicides on sexuality and sexual pleasure.
- impact of microbicides on situations of sexual violence.
- implications for sex trade workers.
- acceptance of microbicides use within same sex couples.
- acceptance of microbicides use within heterosexual couples and the realities of women using microbicides covertly versus negotiating their use with their male partners.

It will only be used as much as the local people want it. Theoretically, women can use it covertly but it is an assumption that may be not as practical in families and in real life. Wives may not be as free as we think they will be. Even with existing family planning products (e.g., birth control pills), there are challenges. Married women always have a different situation. People still have a mental block around being able to use something that connotes mistrust and being unfaithful with their partners. (Interview #1)

2) Engage the Women's Health Sector

- Targeted efforts are needed within all research, policy development and community mobilization efforts to build engagement and collaboration from the women's health movement, the public health sector, and the gay men's health movement. All actions on microbicides should be inclusive of organizations working in women's reproductive health and sexual rights movements and target the messages accordingly.

If there's ever an issue to bridge HIV/AIDS work and the women's health movement, microbicides is it. (Interview #12)

3) Engage the Gay Men's Health Sector

- Targeted efforts are needed within all research, policy development and community mobilization efforts to build buy-in from the gay men's health movement. All actions on microbicides should be inclusive of organizations working with gay men and other men who have sex with men and target the messages accordingly.

Rectal use of microbicides needs special attention because the rectum and vagina are very different biological environments. It's a contentious statement to make that microbicides will be good for both. We need to make sure that we are adequately representing the level of R&D for vaginal and rectal microbicides. There are too many assumptions out there, so we need to make sure that we're not making promises or creating expectations that can't be lived up to. (Interview #10)

- Efforts to engage the gay men's health sector must be framed in alignment with the focus on advocating for a female-controlled prevention tool, and not seen as an opposing movement.

4) Conduct Clinical and Behavioural Research on the Usability of Microbicides

There are a myriad of research issues that need to be addressed with respect to designing microbicides and delivery mechanisms that will be acceptable and useable for women. Specific research issues around usability for women include (but are not limited to):

- lessons learned with respect to other "female-controlled" contraceptive technologies or preventive devices (e.g., birth control pills, female condoms, diaphragms or cervical caps).
- consider issues that women will be concerned about, such as number of hours that a microbicide would be effective, effect of menstrual cycles, and the form in which they would be available.
- efforts need to be made to increase women's comfort with their vaginal anatomy, as they will have to be able touch themselves and insert the product. There may be some important lessons to be learned from early efforts to introduce tampons and female condoms on the market.

We should learn from female condoms – women don't like them for a whole lot of reasons. Microbicides would be so much more manageable and discreet/unobtrusive. Microbicides could be so powerful to women in the sense of being able to use them without knowledge of their partner. It's one of the arguments for making them easily accessible, can be used easily and in circumstances where someone isn't able to negotiate condom use or other protection. Women would buy that argument. (Interview #3)

5. Develop Appropriate Microbicide Promotion Messages

In collaboration with experts in health messaging for sexual health issues for women (e.g., the Canadian Women's Health Network), efforts should begin well ahead of microbicide availability to develop promotion and marketing messages that:

- don't create assumptions that microbicides promote promiscuity.
- target microbicides promotion to both men and women and don't assume that women will always use microbicides covertly. Messages should also encourage men to ask their male or female partners to use a microbicide.
- promote microbicides as a tool in providing a more comprehensive range of prevention options, integrating messages about microbicides into all kinds of HIV/STI education, support, peer counseling, reproductive counseling, post-test counseling, educational campaigns.

- discuss microbicides as building greater autonomy in sexual relationships, especially for women, but without alienating or vilifying men.

Microbicides promotion could feed into the old concern that it just equips women to have sex with anybody. The argument would have to be tailored very carefully. (Interview #26)

There will be the same cultural and social barriers as with condoms, common to all issues around women's reproductive health and sexual rights. There's the religious right which believes that we shouldn't have a right to birth control or abortion or any decisions about sexual health, and therefore shouldn't be using microbicides. (Interview #12)

- share information about the implications of microbicides for prevention of HIV, STIs or unintended pregnancies.
- include information and capacity building efforts about negotiating sexual relationships.
- target people living with HIV in terms of microbicides helping to protect their partner, including issues of disclosure.
- with respect to rectal use of microbicides, ensure that messages don't focus solely on gay men but also reflect that fact that anal sex also occurs within heterosexual contacts.

We need to make sure we position promotion of rectal microbicides as part of the whole microbicides movement and make it clear that women have anal sex too. Rectal microbicides will be just as important for women as gay men. In absolute numbers, there are more women having anal sex than gay men. This is certainly a concern for us as advocates, we have to be careful that we don't play into that false dichotomy in our messages. (Interview #15)

6. Frame Microbicides in the Context of Overall Efforts to Build Sexual Autonomy

Messaging and distribution of microbicides should be contextualized within broader efforts to build reproductive rights, individual choice and sexual autonomy. Of course, the broader societal goal is to work towards equality and respect within all sexual relationships. The discourse around microbicides should be carefully crafted to frame microbicides as offering a prevention tool as “empowerment for the less powerful person in relationships - either gay men or male-female relationships.” (Interview #4)

Appendix A

Consultation Interview Participants for Development of Canadian Microbicides Action Plan

SECTOR	NAME	ORGANIZATION
community	Kevin Perkins	CPAR and CAP AIDS
community	Randy Jackson	Canadian Aboriginal AIDS Network
community	Linda Capperauld	Canadian Federation for Sexual Health
community	Jennifer Kitts	Action Canada for Population and Development
community	Louise Binder	Canadian Treatment Action Council
community	Aideen Reynolds	Pauktuutit Inuit Women of Canada
community	Esther Tharao	Women's Health in Women's Hands
community	Trevor Gray	PASAN
community	Kevin Barlow	Canadian Aboriginal AIDS Network
community	Danielle Layman-Pleet	Voices of Positive Women
community	Janet Madsen	Positive Women's Network
community	Maria McIntosh	AIDS Coalition of Nova Scotia
global partner	Zari Gill	World Vision Canada
global partner	Michelle Munroe	CARE Canada
global partner	Jim Pickett	AIDS Foundation Chicago
global partner	Sumita Banerjee	International Council of AIDS Service Organizations
global partner	Anna Forbes	Global Campaign for Microbicides
global partner	Dr. Henry Gabelnick	CONRAD
global partner	Elisha Maricho	Southern Africa AIDS Training Program (SAT)
global partner	Judith Sullivan	CIDA, Tanzania program
global partner	Polly F. Harrison	Alliance for Microbicide Development
government	Michael Rekart	BC Centre for Disease Control, STD/AIDS
government	Ingrid Wellmeier	HIV/AIDS Policy, Coordination and Programs Division, Public Health Agency of Canada
government	Marc-André LeBlanc	Health Canada, International Affairs Directorate
government	Ian Chisholm	Intellectual property and patents, Health Canada
government	Brian Foster	Therapeutic Products Directorate - Health Products Food Branch, Health Canada
government	Barbara Jones and Robert Lerch	Community Acquired Infections Division
government	Marita Killen	International Affairs Directorate, Health Canada
government	Chris Armstrong	Canadian International Development Agency
Industry	George G. Usher	Polydex Pharmaceuticals Limited
Industry	Jens Van Roey	Tibotec Virco Pharmaceutical Ltd, a subsidiary of Johnson & Johnson
Research	Jacqueline Gahagan	Dalhousie University
Research	Mark Wainberg	McGill University AIDS Centre

SECTOR	NAME	ORGANIZATION
Research	Ken Rosenthal	McMaster University, Canadian Association for HIV Research
Research	Rabeea F. Omar	Université Laval
Research	Michel G. Bergeron	Université Laval, Centre de Recherche en Infectiologie
Research	Stephen Moses	University of Manitoba
Research	Jennifer Gunning	Canadian Institute of Health Research
Research	Martin Méthot	International Partnership for Microbicides