

MICROBICIDES SYMPOSIUM

SYMPOSIUM SUR LES MICROBICIDES

*Volunteer Canada/Bénévoles Canada
330, rue Gilmore Street Ottawa, ON*

OCTOBER 30, 2003/LE 30 OCTOBRE 2003

Canadian AIDS Society  Société canadienne du sida

 Canadian International Development Agency Agence canadienne de développement international


CIHR IRSC
Canadian Institutes of Health Research / Instituts de recherche en santé du Canada
Institute of Health Research / Institut des maladies infectieuses et immunitaires


CIHR IRSC
Canadian Institutes of Health Research / Instituts de recherche en santé du Canada
Institute of Infection and Immunity / Institut des maladies infectieuses et immunitaires


Global Campaign FOR Microbicides

 Health Canada Santé Canada

Interagency Coalition on AIDS and Development  Coalition interagence sida et développement

 INTERNATIONAL PARTNERSHIP for MICROBICIDES

PROCEEDINGS OF THE MICROBICIDES SYMPOSIUM

OTTAWA, ONTARIO — 30 OCTOBER 2003

CO-SPONSORS:

Canadian AIDS Society (Microbicides Advocacy Group Network)

Canadian Institutes of Health Research (Institute of Infection and Immunity)

Canadian International Development Agency

Global Campaign for Microbicides

Health Canada (International Affairs Directorate)

Interagency Coalition on AIDS and Development

International Partnership for Microbicides

The Interagency Coalition on AIDS and Development is a coalition of over 135 Canadian international development non-governmental organizations (NGOs), AIDS Service Organizations (ASOs), faith-based organizations, educational institutions and individuals involved in HIV/AIDS and development issues. The vision of ICAD is a world where the stigma, discrimination and inequities that drive HIV infection are eliminated and people living with or vulnerable to HIV infection are resourced and supported. ICAD's mission is to lessen the spread and impact of HIV/AIDS in resource-poor communities and countries by providing leadership and actively contributing to the Canadian and international response.

ICAD would like to thank the cosponsoring organizations for making this important symposium possible. In addition we would like to acknowledge and thank the symposium planning committee, moderators, panel presenters and event organizers.

Christopher Armstrong	Canadian International Development Agency
Michel G. Bergeron	Université Laval
Mark Bisby	Canadian Institutes of Health Research
David Garmaise	Symposium recorder and author of summary report
Jennifer Gunning	Canadian Institutes of Health Research
Lori Heise	Global Campaign for Microbicides
Polly Harrison	Alliance for Microbicide Development
Marita Killen	Health Canada (International Affairs Directorate)
Marc André LeBlanc	Canadian AIDS Society (Microbicides Advocacy Group Network)
Shari Margolese	Canadian Treatment Action Council
Martin Méthot	Health Canada (International Affairs Directorate)
Bruce Moor	Canadian Institutes of Health Research (Institute of Infection and Immunity)
Stephanie Nixon	International AIDS Vaccine Initiative
Michael O'Connor	Interagency Coalition on AIDS and Development
David Patterson	Canadian HIV/AIDS Legal Network
Zeda Rosenberg	International Partnership for Microbicides
Gail Steckley	Health Canada (International Affairs Directorate)
Esther Tharao	Women's Health in Women's Hands
Karl Tibelius	Canadian Institutes of Health Research
Oline Twiss	Conference organizer
George Usher	Polydex Pharmaceuticals
Marin Van Vliet	Conference organizer
Mark Wainberg	McGill University
Christina Zarowsky	International Development Research Centre

Please contact the presenters directly to request copies of their full presentations. Additional copies of this report can be obtained by contacting

Interagency Coalition on AIDS and Development

1 Nicholas Street, Suite 726
Ottawa, ON, Canada K1N 7B7

Tel: (613) 233-7440

Fax: (613) 233-8361

Email: info@icad-cisd.com

Web: www.icad-cisd.com

TABLE OF CONTENTS

INTRODUCTION	1
WELCOMING REMARKS	3
PANEL 1: OVERVIEW OF THE FIELD	4
PANEL 2: UNDERSTANDING THE MICROBICIDES LANDSCAPE	8
PANEL 3: WHY SHOULD CANADA INVEST IN MICROBICIDES RESEARCH?	11
PANEL 4: THE WAY FORWARD: WHAT CANADA CAN DO	16
WORKING GROUPS: CHALLENGES AND PRIORITY ACTIONS	20
CLOSING REMARKS	23
CONTACT INFORMATION FOR SYMPOSIUM COSPONSORS	24

INTRODUCTION

This one-day symposium brought together people working on, and interested in, microbicide research and development, both from within Canada and from other countries. The symposium consisted primarily of a series of panel presentations, with opportunities for discussion. As well, there was a small group session of facilitated discussion that identified challenges and areas for priority action.

These proceedings provide a synopsis of the presentations made at the symposium; summaries of the main points raised during the discussions on the presentations; and a summary of the outcomes of the small group session.

WELCOMING REMARKS

MARK BISBY — CANADIAN INSTITUTES OF HEALTH RESEARCH

Microbicides have the potential to reduce HIV transmission and to empower women to have more control over their health. The objectives of this symposium are to raise awareness about the potential of microbicides, and to provide opportunities for networking and collaboration.

In the past, the Canadian Institutes of Health Research (CIHR) has not been significantly involved in microbicide research. We are hopeful that this will change; the timing of this symposium is fortuitous in that respect. CIHR is in the process of establishing an HIV/AIDS research advisory committee; this committee will advise CIHR concerning priority research areas. A big challenge, of course, will be to find sources of funding.

The time is right to move the agenda forward on microbicides and the right people are in the room to make it happen.

With sufficient financial resources, strategic partnerships and product development expertise, an effective microbicide that is accessible to women in developing countries is achievable within this decade.

PANEL 1: OVERVIEW OF THE FIELD

The panel was moderated by Karl Tibelius of CIHR. This section contains a synopsis of the presentations made by the two panellists, followed by a summary of the main points raised during the ensuing discussion.

ZEDA ROSENBERG — INTERNATIONAL PARTNERSHIPS FOR MICROBICIDES

Microbicides are needed because:

- almost 50 percent of new HIV infections are among women (55 percent in sub-Saharan Africa);
- most infections are spread by unprotected sex;
- young women are increasingly vulnerable;
- the male condom is under the control of the male partner;
- we need something that women can control; and
- we need something that allows women to live their lives fully, including bearing children.

Microbicides can work in different ways:

- they can cover the surface of the vagina, thus preventing the virus from getting through;
- they can attack the virus itself; and
- they can stop the virus from adhering to cells.

Microbicides could take the form of a gel or cream, a film, a suppository, a sponge or vaginal ring slowly releasing the active ingredient, or some new formulation.

In terms of clinical testing, many candidate products have been tested in phase I trials, some have progressed to phase II trials, and only a few have made it to phase III trials. There have been a number of important lessons learned from these trials, but there are no surrogate markers yet for efficacy and we are still searching for “proof of concept.” It is challenging to do a placebo-controlled trial.

Nonoxynol-9 is the only product to make it through phase III trials, but it has been shown to be too toxic. Six other products are poised to go into phase III trials in 2004. The idea is to have an uninterrupted pipeline of products in the testing pipeline, but increased resources are needed to make this happen. There is an absence of pharmaceutical industry investment. No existing organization has the capacity to survey and assess all of the products in the pipeline and implement a plan for the rapid development of promising candidates.

The goal of the International Partnership for Microbicides (IPM) is to accelerate the discovery, development and accessibility of safe and effective microbicides. We are looking for products that are effective and that can be developed and made available quickly. With sufficient financial resources, strategic partnerships and product development expertise, an effective microbicide that is accessible to women in developing countries is achievable within this decade.

LORI HEISE — GLOBAL CAMPAIGN FOR MICROBICIDES

The Global Campaign for Microbicides (GCM) is an international coalition of NGOs working collaboratively to:

- raise awareness and mobilize political will for increased funding for microbicide research and eventual access;
- create a supportive policy and user environment for the timely development, introduction and use of new prevention technologies; and
- ensure that as science proceeds, the public interest is protected and the rights and interests of trial participants, users, and communities are fully represented and respected.

Products currently being tested have a number of attractive features:

- Some products being investigated prevent pregnancy; others do not.
- Many candidate products are widely anti-microbial and could provide protection against a range of STDs.
- Microbicides would help protect men as well as their female partners.
- 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.

Microbicides would be promoted as an adjunct or back-up to condoms, not as a replacement.

Once a microbicide is available, prevention messages would shift to a hierarchy of options, such as:

- Use a male or female condom every time you have sex; if you absolutely can't use a condom, use a microbicide.
- Use a microbicide with your condom for added pleasure and protection.

Alternatively, microbicides could be promoted specifically for use with regular partners.

Studies in countries in southern Africa show that reported levels of condom use in marital, cohabiting partnerships are extremely low, and that reported levels of condom use among casual partnerships, while higher, are still consistently below 50 percent. Multiple studies reveal a high degree of interest in microbicides and indicate that microbicides would be acceptable to women and most men.

Men and women who practice anal sex also need a safe and effective microbicide. It will be more challenging, for biological reasons, to create an effective rectal microbicide. At a minimum, we must ensure that microbicides developed for vaginal use are safe for rectal use because they *will* be used that way.

Multiple studies reveal a high degree of interest in microbicides and indicate that microbicides would be acceptable to women and most men.

One group of researchers has estimated that a 60 percent efficacious microbicide introduced into 73 low income countries would avert 2.5 million HIV infections over three years in women, men and infants.

About 60 small biotech companies and non-profit researchers are actively engaged in microbicide research and development (R&D), but they rely on government and foundation grants to develop their products. There are about 55 leads under development. “Big Pharma” has been unwilling to invest in early microbicide R&D because:

- there is a perception that only poor people need this product;
- there are concerns about liability and regulatory uncertainty;
- there is a belief that the potential global market is small; and
- there is a relative disinterest on the part of most companies in non-prescription drugs.

In short, Big Pharma is not investing because it is not in their (short term) economic self-interest to do so. However, second or third generation products may be profitable, so the long-term market should be sufficient to attract private investment. In the meantime, public subsidy will be required to bring the first generation of microbicide to market. This means that advocacy for government and donor funding is essential.

How much will it cost? It is estimated that pre-clinical and clinical research will cost about US\$46.4 million per product. One model estimates that it would take US\$775 million over five years to achieve a high likelihood of getting one or more products by 2010. This estimate does not include costs related to discovery of new leads, work on access or advocacy, or organizational overhead. Moreover, it assumes that all leads are controlled and managed by one entity – as if the world operated like a pharmaceutical company. In FY 2002, the National Institutes for Health, by far the largest source of funding for microbicide research, invested an estimated US\$55.7 million in microbicide R&D. This represented only two percent of the Institute’s AIDS-related research budget.

One group of researchers has estimated that a 60 percent efficacious microbicide introduced into 73 low income countries would avert 2.5 million HIV infections over three years in women, men and infants. This estimate conservatively assumes that:

- the microbicide is effective only against HIV, not other STDs;
- the microbicides is taken up by only 20 percent of individuals already in contact with services; and
- those who use microbicides do so in 50 percent of acts where they do not use condoms.

So, even a relatively low efficacy microbicide could have a large impact on the epidemic.

Concerns have been raised about introducing a method that is less efficacious than condoms. Will individuals default from condoms to microbicides because they are easier to use? Three lines of evidence suggest that introducing microbicides will lead to *more* protection rather than *less*.

First, experience from family planning has shown that the addition of each new method *increases* the overall number of protected acts and decreases unintended pregnancies. Second, the majority of research studies on condom migration reveal that the availability of additional protection actually increased consistent condom use. Finally, one mathematical modeling study suggested

that under most circumstances, substantial migration can be tolerated without increasing risk either at the level of individuals or of sub-populations. The study predicted that migration would potentially be a problem only where condom use is high (> 70%) and achieved microbicide consistency is low (< 50 % of non-condom protected acts).

We need to work now to anticipate and address cultural issues with respect to the use of microbicides

The microbicide issue exists at the confluence of two historical trajectories: women's health movement and AIDS activism. The idea evolved from needs expressed by grassroots women; the AIDS leadership came later. The current momentum is due largely to the sustained activism of the past decade. Sustained civil society engagement is as critical to success as investment in scientific leadership.

DISCUSSION

The following points emerged from the discussion:

- Women are very interested in microbicides. They get angry about the fact that microbicides are not yet available, and they are demanding to participate in the clinical trials. It is harder to inject this sense of urgency into the policy and donor community.
- Microbicides may enhance the sexual experience. We need to promote the positive aspects of microbicides and not just treat this as a negative disease model.
- With respect to possible toxicity and harmful effects on a fetus, more research is needed on the safety of microbicide use during pregnancy. This will take time. In the meantime, it is safer to assume that there will be some toxicity.
- Some of the microbicides entering clinical trials are likely to benefit men as well as women, but we need to await the results of the clinical trials before we can formally make this claim. We want to be able to promote microbicides to both men and women; this would benefit HIV positive women who want to have sex.
- The current safety trials are looking at safety for both HIV negative and HIV positive women.
- We need to work now to anticipate and address cultural issues with respect to the use of microbicides. It is not clear what stance some faith-based communities will take towards microbicides; we have to keep in mind that some microbicides may not have contraceptive properties. Different approaches will be required in different countries. The country preparedness studies that will be done will help to deal with this issue.
- With respect to working with developing country governments: (a) discussions are happening concerning what the researchers will give back to the countries and communities where trials are done; (b) there have been discussions about doing twinning programs in order to transfer technology to developing countries; (c) Community Advisory Boards are set up for each trial; and (d) grants are often given to partner organizations in-country so that they can talk to their governments. A lot more still needs to be done.
- Microbicides will not replace the female condom. What women need are more choices. But the female condom has its limitations; it is perceived as a physical barrier.

The synergistic nature of HIV vaccines and microbicides means that a microbicides-vaccine alliance would be quite productive

-
- More work needs to be done to sort out the intellectual property issues with respect to microbicides. The IPM tries to build in safeguards in its agreements to ensure that the product will be widely available and accessible.

PANEL 2: UNDERSTANDING THE MICROBICIDES LANDSCAPE

The panel was moderated by Zeda Rosenberg of the IPM. This section contains a synopsis of the presentations made by the three panellists, followed by a summary of the main points raised during the ensuing discussion.

MARC-ANDRÉ LEBLANC — CANADIAN AIDS SOCIETY

The Microbicides Advocacy Group Network (MAG-Net) is a coalition of about 30 Canadian AIDS service organizations, sexual and reproductive health organizations, international development NGOs and researchers. It is coordinated by the Canadian AIDS Society (CAS) and serves as the Canadian arm of the GCM.

The goals of MAG-Net are:

- to share ideas and resources on raising awareness of microbicides with other CAS members and partners; and
- to share ideas and provide input into coordinated advocacy efforts at local, national and global levels.

Key activities of MAG-Net include developing a Community Mobilization Kit; raising awareness in communities; mobilizing support for microbicide research and development; interacting with Health Canada and the Canadian International Development Agency to promote microbicides; taking steps to address issues around Nonoxynol-9; and preparing a discussion paper on ethical and legal issues with respect to microbicides. The discussion paper will recommend that Canada develop a Canadian Microbicides Plan.

STEPHANIE NIXON — INTERNATIONAL AIDS VACCINE INITIATIVE

The mission of the International AIDS Vaccine Initiative (IAVI) is to ensure HIV vaccine development and delivery, which means participating in R&D efforts, but also working on the political, policy and community environments in the North and South to ensure that HIV vaccines are developed and delivered as quickly as possible. It is in IAVI's interest to advocate for enhanced support for microbicide development and delivery because IAVI can achieve its own mandate faster by forging strategic alliances. The synergistic nature of HIV vaccines and microbicides means that a microbicides-vaccine alliance would be quite productive.

Investing in both HIV vaccines and microbicides will create an outcome that is greater than the sum of its parts for a number of reasons, including the following:

- Existing prevention approaches (i.e., abstinence, and the male and female condoms) can be effective where available, but they have limitations in terms of: (a) how easy they are to use; (b)

the options they provide to women; (c) the options they provide in terms of family planning; (d) the difficulties in sustaining their use; and (e) the presence of significant cultural or religious barriers. The severity of the epidemic demands that we maximize our chances of success by finding new tools. People need more choices in order to protect themselves and their partners.

People working on vaccines and microbicides should be strategizing on innovative ways to ensure ready access to new products as they are developed

- Microbicides and vaccines will be two extremely significant additions to the arsenal of HIV prevention strategies. However, neither one is enough by itself. At an individual level, acceptability, uptake and sustained use of these different HIV prevention approaches will vary considerably in different places and at different times.
- It is unlikely that any single approach will be 100% effective at first.
- Basic science advances that enhance our understanding of mucosal immunity should help both vaccine and microbicide research and development.
- Both products face an uncertain market and a non-guaranteed return, which poses a challenge to investment. Vaccine and microbicide advocates can work together to develop strategies to engage the small biotechnology firms that are often the ones involved in the early stages of taking research forward.
- Recruitment and retention and follow-up of large, high-risk, HIV-negative cohorts is a challenge for both vaccine and microbicide trials. There are also lessons to be learned jointly with respect to ensuring meaningful community participation in trials.
- People working on vaccine and microbicide trials face other common issues, such as: (a) the need to ensure that consent to participate in the trials is truly voluntary and informed; (b) the need to develop appropriate prevention education programs in communities where the trials are being held; (c) the need to ensure that referrals and services are available for people who are found to be HIV-positive during screening for participation in the trial; (d) the need to determine an appropriate standard of care to be provided during and after the trial to participants and their families; (e) the need to address the perceived or actual effect of the trial on pregnancy and family planning; and (f) the need to address issues of liability in terms of teratogenic effects, real or perceived, in the case of birth defects for product users.
- People working on vaccines and microbicides share the challenge of enhancing the technical capacity of countries for developing national plans for conducting vaccine and microbicide trials; and for the financing, distribution and use of products. Even though countries may develop separate plans, the lessons and efforts should be shared.
- Products in both the vaccine and microbicide families require global regulatory preparation spanning preclinical and clinical development, and possibly even anticipating post-licensure needs.
- Once there are both vaccine and microbicides available, people in both fields will need to work together to estimate demand for the products, including measuring the impact of a new product on demand for existing products.
- People working on vaccines and microbicides should be strategizing on innovative ways to ensure ready access to new products as they are developed.

AMD estimates that each new product in the pipeline will need an investment of about US\$273 million to go through all stages of clinical testing and to complete preparedness studies

POLLY HARRISON — ALLIANCE FOR MICROBICIDE DEVELOPMENT

The Alliance for Microbicide Development (AMD) was founded in 1998 as an agent of change, at a time when progress on microbicides was slow, fragmented and under-funded. Now the AMD is a coalition of over 200 representatives from scientific research institutions, small bio-pharmaceutical companies and health advocacy groups; plus about 300 “colleagues” (people who just want to receive AMD materials). The AMD is increasingly global in scope.

The AMD acts as a catalyst, communicator, convener, problem-solver and partner. The work of the AMD includes:

- informing, educating and communicating (through websites, publications, information kits, presentations and media briefings);
- tracking the microbicide pipeline;
- expanding the funding base;
- clarifying and influencing the regulatory processes;
- convening broadly representative meetings;
- planning, participating in, and presenting at, conferences;
- researching critical issues;
- problem-solving and brokering collaborations; and
- “watchdogging” events and issues threatening the field.

Key achievements of the AMD include:

- creating a microbicides “field;”
- increasing the funding base;
- having an impact on public policy and legislation; and
- enhancing the responsiveness to microbicides at key US agencies.

Considerable progress has been made in the last few years, including:

- The pipeline of products is growing.
- The image of microbicides is improving.
- New scientists have been enticed into the field.
- The number of peer-reviewed articles has increased significantly.
- The advocacy base is bigger and wider, yet more integrated.
- There is better interface between advocates, scientists and developers.
- Microbicides have been recognized as one of the 10 most promising biotechnologies for improving global health.

With respect to funding, investment in microbicides R&D from the public and private sectors has increased steadily from US\$28.2 million in 1997 to an estimated US\$158.1 million in 2003. The AMD estimates that each new product in the pipeline will need an investment of about US\$273 million to go through all stages of clinical testing and to complete preparedness studies. This does not include other costs, such as pre-clinical, regulatory and advertising.

DISCUSSION

The following points emerged from the discussion:

- There is substantial interest in microbicides among women in both the United States and Canada. There are 10 sites (“nuclei”) in the US and one site in Canada (MAG-Net) where women are actively advocating for microbicide research and development. However, more could be done to build constituencies around this issue.
- There are definite linkages between vaccines and microbicides, and areas where the two fields should be working together. But there are also differences, so it may not make sense to push for an integrated Canadian vaccine and microbicide plan. Strengthening both areas of research can be mutually reinforcing.
- The WHO is now focusing more on microbicides and is about to form a task force.
- While IAVI and the various microbicide groups do not have a formal relationship, there is a lot of collaboration and personal interaction between the two. IAVI was used as the model for structuring the IPM.
- Organizations representing women’s health, family planning and HIV/AIDS need to work together more closely to promote microbicides.
- The manufacturing challenges are far fewer for microbicides than they are for vaccines.

The manufacturing challenges are far fewer for microbicides than they are for vaccines

PANEL 3: WHY SHOULD CANADA INVEST IN MICROBICIDE RESEARCH?

The panel was moderated by Michael O’Connor of the Interagency Coalition on AIDS and Development. This section contains a synopsis of the presentations made by the four panellists, followed by a summary of the main points raised during the ensuing discussion.

ESTHER THARAO — WOMEN’S HEALTH IN WOMEN’S HANDS

HIV/AIDS increasingly affects women in Canada, particularly women in prison, Aboriginal women and black women. Aboriginal and black people are over-represented among reported AIDS cases. HIV infection rates among communities from sub-Saharan Africa and the Caribbean living in Ontario is about 12 percent, a rate surpassed only by men who have sex with men. HIV prevalence in the black community in Ontario has increased by 85 percent since 1996.

However, even with such high infection rates African and Caribbean communities, particularly women, have played a very limited role in HIV/AIDS services and programs. This led to a decision to undertake the study on the “The Silent Voices of the HIV Epidemic: African and Caribbean Women”. The women in the study described themselves as:

- culturally and racially entrenched and not fully integrated into the Canadian society; and
- living in traditional, religious and patriarchal structures located within a western society.

Most women have no control over whether their partners choose to use condoms or not.

-
- The women identified the following factors that put them at risk for HIV infection:
- individual and community views about the disease;
 - racism;
 - competing priorities in women's lives;
 - gender issues (including violence against women, lack of communication between partners, women's dependence on men, and women lacking power in relationships);
 - cultural and religious practices, values and beliefs;
 - discrimination against HIV positive women; and
 - homophobia.

The study illustrated how broader factors influence individuals' behaviours and choices. Socio-economic factors, gender, cultural and religious values, and beliefs and practices play an important role in women's ability to protect themselves from HIV infection. HIV-related stigma and other types of discrimination further compound the issue by increasing the inability of women to protect themselves. Many prevention strategies focus on individual behaviour change, neglecting the broader factors that influences individual and community behaviours. Most women have no control over whether their partners choose to use condoms or not. Neither do they have control over the broader factors that have direct influence on their risk of HIV infection. Therefore, women need to be provided with prevention options they can control – options such as microbicides.

**DAVID PATTERSON — CONSULTANT, CANADIAN HIV/AIDS
LEGAL NETWORK**

By the closing plenary of the Barcelona Conference, two headline messages had emerged: (a) that rapid scale-up of the provision of antiretroviral therapies (ARVs) in resource poor settings is an achievable global priority; and (b) that the delivery of prevention and treatments are inseparable goals. We are at an early stage in terms of understanding the full range of the preventive impacts of treatments. However, we can state now that:

- scaling up treatment provides the best environment for future prevention;
- treatment provision is necessary if we are to involve persons living with HIV/AIDS as prevention advocates;
- treatment access strengthens the health sector (through higher skills levels, greater community confidence, workforce survival);
- a strong health sector is necessary to deliver vaccines; and
- treatment access reduces stigma and supports HIV testing.

Globally, activists are working to integrate aspects of treatment and prevention advocacy. The Canadian HIV/AIDS Legal Network has undertaken a project to:

- review commonalities and differences of the activist movements;
- apply a human rights framework;
- map intersecting agendas; and
- propose a joint agenda for action.

Global treatment, vaccines and microbicides advocates are meeting in Montreal in November 2003. (A report from this meeting will be available in early 2004.) If these advocates are going to work together in future they will need to overcome barriers such as:

- institutional separation (i.e., issue specific NGOs);
- different political sub-cultures;
- a history of competition for funding, R&D resources and the media limelight; and
- different timeframes (treatments: now; vaccines and microbicides: long haul).

We need to apply a rights-based approach. The right to health means that new prevention and treatment options need to be pursued concurrently.

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

- 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 community education on joint treatment/prevention packages;
- empower communities (e.g., sex workers and drug users) to engage in community debates and decisions about trials;
- 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.

In the area of policy, treatment and prevention, advocates can work together to:

- promote a new pro-poor deal for global R&D;
- scrutinize free trade agreements to ensure that the right to health is not compromised by intellectual property rights; and
- promote open collaborative models of innovation for HIV biotechnologies.

Equity pricing, financing and bulk procurement for ARVs for developing countries will pave the way for access to vaccines and microbicides.

The right to health means that new prevention and treatment options need to be pursued concurrently.

If the demand for microbicides in Canada is so evident to our community, then why is it not evident to policy makers? Why is there not more microbicide research and development?

SHARI MARGOLESE — CANADIAN TREATMENT ACTION COUNCIL

From the community perspective, the role of Canadian advocacy in supporting microbicides is not unlike the role of advocacy in access to treatment. HIV/AIDS treatment and prevention educators have long been aware that women and men who have sex with men need a new tool in their arsenal to fight HIV, a tool that they can control without having to rely on their partners' cooperation. The community-based AIDS movement has taken the lead in microbicides advocacy in Canada.

If the demand for microbicides in Canada is so evident to our community, then why is it not evident to policy makers? Why is there not more microbicide research and development? One reason is likely limited resources. The work of advocating for microbicides in Canada has fallen to community-based organizations whose resources are already stretched to the limit. Ideally, the role of Canadian advocacy on microbicides would include:

- informing research;
- informing public and private sector policy;
- promoting public awareness;
- providing mentoring and skills building to people living with HIV/AIDS and at-risk communities; and
- encouraging and facilitating the exchange of information amongst relevant stakeholders.

Advocacy to inform research is required to ensure that:

- there is good communication between the community and the researchers;
- vulnerable communities are represented in research;
- trial designs are appropriate for the communities involved;
- both the trial and the informed consent form meet ethical criteria; and
- community advisory boards or other mechanisms of citizen engagement are available.

In terms of public and private sector policy, Canada has an opportunity to play a global leadership role in microbicides development. It is the role of advocates:

- to inform our government and pharmaceutical partners of the demand for microbicides both in Canada and globally, and to demand that they invest in microbicides research;
- to ensure that government and pharmaceutical company regulations, policies and practices regarding drug pricing will make microbicides available and affordable; and
- to ensure that a meaningful post-approval surveillance system is in place to track the use of microbicide after they hit the market.

Even before a microbicide is brought to market in Canada, it is the role of advocates to promote the need for the product, and the acceptability and appropriate use of the product; and to act as watchdogs to protect the public against any false claims of microbicide manufacturers. Community advocates need to raise microbicides awareness among at-risk communities and educate people about clinical trials. The communities at greatest risk often have the least knowledge about microbicides.

It is vital that all stakeholders be at the table to ensure best practices and highest possible standards of care are achieved. Organizing meetings (like the one today) on an ongoing basis will be key to the success of any microbicide advocacy strategy. It is also important to build partnerships, and to encourage discussion of microbicides outside of the HIV community (in the mainstream health community).

It is vital that all stakeholders be at the table to ensure best practices and highest possible standards of care are achieved.

MICHEL G. BERGERON — UNIVERSITÉ LAVAL

It is important to develop safe and effective microbicides under the control of women to help them control their sexual destiny. The Invisible Condom,TM which is being developed by the Infectious Diseases Research Centre at Université Laval, is a microbicidal thermo-reversible gel formulation designed to prevent the sexual transmission of HIV/AIDS and other sexually transmitted infections (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 *vitro* has shown that the gel can prevent HIV and other STIs. Experiments with mice have also yielded promising results. Four phase I trials have been completed. The trials revealed that:

- there was no change in the presence of lactobacillus in the vagina, a substance 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 highly acceptable to women.

Other factors that make the Invisible CondomTM unique are that it is tasteless and odourless, that its presence is imperceptible, and that there is no vaginal leakage. Phase II trials of the Invisible CondomTM will be done as soon as the anticipated funding comes through. A protocol has already been written for a phase III trial.

We need to explore how best we can work together to develop a collaborative framework to support policy, program, research and funding mechanisms for microbicide research.

DISCUSSION

- The following points emerged from the discussion: It is not clear whether the microbicides that are eventually marketed will be classified as drugs. If prescriptions are required to obtain the microbicides, this may significantly discourage their use. On the other hand, the microbicides may have to be considered as drugs until we are sure that they are safe enough to be sold over the counter.
- If one or more ARVs were added to a microbicide, then it would certainly be classified as a drug. But it may not be a good idea to go this route because of potential problems with resistance. Determining exactly how the intellectual property issues around microbicides will be identified will be a major challenge. IAVI has used innovative contracts to ensure that any successful products will be made available at reasonable prices. We should document how IAVI did this and see how its process can be applied to microbicides.

PANEL 4: THE WAY FORWARD: WHAT CANADA CAN DO

The panel was moderated by Gail Steckley of Health Canada. This section contains a synopsis of the presentations made by the five panellists, followed by a summary of the main points raised during the ensuing discussion.

CHRIS ARMSTRONG — CANADIAN INTERNATIONAL DEVELOPMENT AGENCY

The Canadian International Development Agency (CIDA) launched an HIV/AIDS Action Plan in July 2000. Prevention and R&D are two programming areas in the Action Plan.

In April 2000, CIDA, in collaboration with Health Canada, provided funding in the amount of \$350,000 to Laval University for a phase I clinical trial of a microbicidal gel. CIDA continues to be supportive of research and development initiatives that focus on health issues prevalent in developing countries, including research into products that enable one of the most vulnerable populations, young girls and women, to have access to interventions that will inhibit the sexual transmission of HIV and other STIs.

We need to explore how best we can work together to develop a collaborative framework to support policy, program, research and funding mechanisms for microbicide research. We also need to explore opportunities to use leveraging to advance the microbicide research agenda. One forum where this could happen is the International AIDS Conference in Bangkok, Thailand in 2004.

Up to now, CIDA's contribution to research efforts has mostly been through multilateral mechanisms. CIDA is not in a position at this time to support more work around microbicides, but is looking for opportunities to do so in future.

BRUCE MOOR — CANADIAN INSTITUTES OF HEALTH RESEARCH

CIHR supports outstanding health research in Canada, encourages multidisciplinary team research approaches, and seeks to increase Canadian research capacity in areas where opportunities for growth exist. The Institute of Infection and Immunity, one of the thirteen institutes of the Canadian Institutes of Health Research (CIHR), targets diseases that cause much patient suffering and have a high cost to the health care system. The Institute supports research in infection and immunity in areas where there is the potential to advance knowledge and make an impact on global health. In particular, HIV/AIDS research is a strategic priority focus for the Institute of Infection and Immunity.

Currently, CIHR is funding one project (part of the Global Health Research Initiative) that is directly relevant to microbicides. Although there is no program specifically designed to support microbicide research, applications in this area are eligible for funding and encouraged in the open grants and awards competitions. In the future, CIHR hopes to be able to advance the microbicides research agenda through the following strategies:

- determine Canadian capacity for research relating to microbicides;
- establish funding partnerships;
- design targeted research funding programs (including ones involving international linkages) that utilize Canadian scientific expertise

MARTIN MÉTHOT — HEALTH CANADA

Microbicides have a 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 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 International Affairs Directorate (IAD) of Health Canada focuses its efforts on trying to complement the work of others; on promoting collaboration, coordination and synergy in the response; and on building linkages between domestic and global experiences. The IAD works with other government departments and agencies to implement the priorities outlined in the UNGASS Declaration of Commitment on HIV/AIDS, which Canada has endorsed, and which include investing in research and development of female controlled methods of prevention and microbicides.

Recently, Health Canada has signed a new partnership agreement with UNAIDS, which commits us to seeking out areas for collaboration, and to contributing our expertise and experience to UNAIDS priority areas.

Microbicides have a place in the broader effort to reduce the spread of HIV/AIDS, both in Canada and globally

Our development teams see the successful development of an effective microbicide as not just a moral imperative, but also a commercial opportunity.

We need to engage with the international research community, and the international community of people living with and affected by HIV/AIDS. For microbicides to be widely accepted and accessible, they will need to be developed with the end users in mind. They will need to be affordable, easy to use, and marketed in such a way that they reach the communities most in need. We need to learn and apply lessons from existing prevention efforts, including successful and unsuccessful efforts to promote condom use, and including our experience with the female condom in Africa, which is still seen as an interesting but not very serious alternative.

We need to be thinking *now* about how to address these issues. As we renew the Canadian Strategy on HIV/AIDS, we are taking this agenda into account as one important piece of the broader federal response. The dialogue we are engaging in today provides a good foundation for this work, and for ongoing consultation on the priorities and approaches that we need to pursue.

GEORGE USHER — POLYDEX PHARMACEUTICALS LTD.

Polydex is a very small company with annual sales in the range of \$13 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.

Microbicide developers need further monetary support now for large-scale clinical trials. As these trials produce results, further development work may be necessary. Ultimately, the end use of an effective microbicide will present even further challenges.

It would be helpful if the large pharmaceutical companies were doing more innovating and less merging; and if governments would ease up on restrictions on how and where to do research. One strategy governments should consider is having grant monies paid back from the profits of successful products.

CHRISTINA ZAROWSKY — INTERNATIONAL DEVELOPMENT
RESEARCH CENTRE

The mandate of the International Development Research Centre (IDRC) is to support research in development. Our primary focus is providing funding to developing country researchers, but we also strongly support partnerships with Canadian institutions and researchers. IDRC's Governance, Equity and Health Program supports research that strengthens health systems and promotes civic engagement. IDRC does not have funds to support basic science research.

With respect to the current state of research on microbicides, there are a number of issues, most of which have to do with power, prevention, pleasure and partnership. One of the power issues is gender: Why are microbicides still under-emphasized? We need strategies to get microbicides more on the agenda, to build microbicides into all kinds of research. Another power issue has to do with biotechnology. Biotechnology research is much better funded than health systems research. We need to figure out how to use biotechnology to support the microbicides agenda. A third power issue is who is doing the research? Can we support more fruitful collaborations between NGOs, university researchers and private corporations? How do we make sure the South is actively involved?

With respect to prevention, one of the issues is how are we going to implement and monitor the roll-out of a successful microbicide? We need to think about how we are going to monitor the impact on areas such as health, social equity and gender relations.

We need to think about what qualities need to be developed in microbicides to respond to the pleasure component of sex. How will we promote something that might be freely distributed in clinics, refugee camps and elsewhere, but which also might be heavily flogged on the market? To the extent that microbicide research involves understanding and acting around sex and sexuality, gender identity, gender roles, livelihoods, family reproduction, etc., this opens up opportunities for collaborative research among different agencies. What are the interfaces between research on sexuality and research on preventive technologies and health systems? There is a lot of thinking that needs to be done about how to make these interfaces. We need to start thinking about this now, because microbicides will be available soon.

Finally, we need to think about how to create partnerships that will advance the microbicides agenda. There are opportunities for funding from IDRC around all of these questions and issues. You need to be creative and you need to be pushy. The coalitions that are forming around microbicides are a welcome development. While IDRC does not have and will not have a specific program on microbicides, it does have research programs that can be tapped.

We need to think about what qualities need to be developed in microbicides to respond to the pleasure component of sex.

More work needs to happen with vulnerable communities, such as the ethnic communities, if we are going to be successful in reaching people in these communities

DISCUSSION

The following points emerged from the discussion:

- To make sure that governments provide more funding for microbicide research and development, the NGO sector needs to keep pushing. Microbicides needs to be on the agenda of the International Working Group on HIV/AIDS, where CIDA, the CIHR and the Department of Foreign Affairs and International Trade are in attendance. It is expected that vaccines and microbicides will have a higher profile in the renewed Canadian Strategy on HIV/AIDS.
- Work done in other fields could inform what needs to be done on microbicides. We need a way to tap into this.
- More work needs to happen with vulnerable communities, such as the ethnic communities, if we are going to be successful in reaching people in these communities with messages about microbicides when they are released on the market.
- It has been difficult to attract people to this field (and to this meeting) who are not already involved in microbicides. We need to find innovative ways of attracting more people, especially scientists. This will remain a major challenge as long as this area remains under-funded.
- In Canada, for the next little while there may be more opportunities in social science research than in basic research.

WORKING GROUPS: CHALLENGES AND PRIORITY ACTIONS

This session was facilitated by David Patterson. Three working groups were formed: one consisting of government people; one consisting of researchers and representatives of academia and industry; and one consisting of community people. Each group was asked to identify some of the key challenges to advancing microbicide research and development, and to recommend some priority actions to overcome these challenges. Each working group then reported back to the full plenary. The following is a synopsis of the challenges and priority actions that were identified by all three groups.

CHALLENGES

- There is insufficient interest on the part of researchers (in all fields) in microbicide research. It is hard to get microbicides on the research agenda and to attract new researchers to the field.
- There are insufficient financial resources to conduct microbicide research, including the “soft” side of microbicides research (particularly funding for clinical trials infrastructure). The fact that government funding in this field is limited leads to competing priorities for what monies are available.
- There is insufficient understanding on the part of the public and the politicians that microbicides are an essential component of prevention.
- Private sector companies are not convinced that there is value in taking on microbicide research and development.

RECOMMENDATIONS FOR PRIORITY ACTIONS

ENGAGING RESEARCHERS

- CIHR should create small requests for proposals to stimulate researchers' interest.
- CIHR should issue a request for proposals for the social and behavioural aspects of microbicide research.
- CIHR should involve its Institute of Gender Health in its efforts to promote microbicide research.
- CIHR should use fellowships and scholarships as a way of promoting more microbicides research and engaging trainees.
- CIHR should provide opportunities for the development of research teams, using mechanisms available at CIHR (such as the Community Alliances for Health Research and the Interdisciplinary Health Research Teams).
- Microbicides should be discussed during a strategic planning session of the Global Health Research Initiative.
- Mechanisms should be found to get basic science researchers in touch with social science researchers to discuss microbicide research issues.
- Pharmaceutical and biotechnology associations should be involved in meetings on microbicides and should be educated about microbicides.

EDUCATION AND AWARENESS

- A short document should be prepared (2-3 pages) making the case why Canada should be involved in microbicides research.
- General and targeted education campaigns should be implemented to effectively position microbicides.
- Articles should be published in newsletters and other media.
- The message should position microbicides as: (a) not just an HIV/AIDS prevention method; and (b) something that will help both a men and women.

COMMUNITY MOBILIZATION

- The community should undertake a broad mobilization campaign to get microbicides on the agenda. The campaign should be directed not only at HIV/AIDS organizations, but also women's health organizations, development organizations and others. Microbicides needs to be mainstreamed. There is a need to get more people talking about microbicides.
- Groups like MAG-Net should be strengthened and expanded.

RESOURCES, POLICY, ADVOCACY

- More resources should be made available for microbicides research and development.
- A national microbicides plan should be developed, parallel to or integrated into a vaccine plan or a broader immunization plan.
- Relevant government departments should get together to strategize about how best to promote microbicide research and development.
- Global lobby efforts should continue (including making microbicides a key part of the next International AIDS Conference in Bangkok).

CLOSING REMARKS

MARTIN MÉTHOT — HEALTH CANADA

This meeting has energized a lot of people. I am sure that everyone here is going to go back home and mention microbicides at least once every day from now on. We need to keep the momentum going. There is now a wave of interest around the world on HIV/AIDS. Those of us who are interested in microbicides need to be riding that wave. There are incredible strengths among the participants of this meeting, which means that we have the tools to promote microbicides.

There will be opportunities in the future – including the International AIDS Conferences in Bangkok in 2004 and Toronto in 2006 – to advance the microbicides agenda. We need to strategize on how best to do this. Hopefully, we will be able to have another forum like this one next year, in advance of the Microbicides 2004 Conference.

CONTACT INFORMATION FOR SYMPOSIUM COSPONSORS

Canadian AIDS Society
(Microbicides Advocacy Group Network)
309 Cooper Street, 4th Floor
Ottawa, ON, Canada K2P 0G5
Tel: (613) 230-3580
Fax: (613) 563-4998
Email: casinfo@cdnaids.ca
Web: www.cdnaids.ca

Canadian Institutes of Health Research
410 Laurier Avenue W., 9th Floor
Ottawa, ON, Canada K1A 0W9
Tel: (613) 941-2672
Fax: (613) 954-1800
Email: info@cihr-irsc.gc.ca
Web: www.cihr-irsc.gc.ca

CIHR Institute of Infection and Immunity
SDRI 214, University of Western Ontario
London, ON, Canada N6G 2V4
Tel: (519) 661-3228
Fax: (519) 661-4226
Email: iii@uwo.ca
Web: www.cihr-irsc.gc.ca/e/institutes/iii

Canadian International Development Agency
200 Promenade du Portage
Gatineau, Québec, Canada K1A 0G4
Tel: (819) 997-5006
Fax: (819) 953-6088
Email: Sandra_Black@acdi-cida.gc.ca
Web: www.acdi-cida.gc.ca

Global Campaign for Microbicides
c/o PATH
1800 K Street NW
Washington, D.C., USA 20006
Tel: (202) 822-0033
Fax: (202) 457-1466
Email: info@path-dc.org
Web: www.global-campaign.org

Health Canada
(International Affairs Directorate)
Health Policy and Communications Branch
Jeanne Mance Building
Tunney's Pasture, A.L. 1903B
Ottawa, ON, Canada K1A 0K9
Tel: (613) 957-7311
Fax: (613) 957-4195
Email: marita_killen@hc-sc.gc.ca
Web: www.hc-sc.gc.ca/datapcb/iad

**Interagency Coalition on AIDS
and Development**
1 Nicholas Street, Suite 726
Ottawa, ON, Canada K1N 7B7
Tel: (613) 233-7440
Fax: (613) 233-8361
Email: info@icad-cisd.com
Web: www.icad-cisd.com

International Partnership for Microbicides
1010 Wayne Avenue, Suite 510
Silver Spring, MD, USA 20910
Tel: (301) 608-2221
Fax: (301) 608-2241
Email: info@ipm-microbicides.org
Web: www.ipm-microbicides.org