

Microbicides - the case for Europe



**Cairde
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Preface:

'If you do not cry out, you will die unheard...'

—Swazi proverb

Twelve years ago, during an international workshop on HIV and AIDS, a Ugandan woman posed the following challenge: "If scientists are clever enough to put a man on the moon, why can't they make an AIDS prevention option that women can control?"

Why indeed?

Since then a rising tide of voices have joined this chorus. More than two decades into the AIDS epidemic, the world is still dependent on the male or female condom for preventing disease. Regrettably, neither is a viable option for many individuals around the world. Given the social, political, and economic forces that condition people's risk, individuals need and want a wider array of tools to enhance their own protection.

One approach on the horizon that deserves increased public and private sector support is topical microbicides. At the present rate of progress, however, it will be 10 years or more before a safe, effective and affordable microbicide becomes available to women and men worldwide. Reducing this time frame will require global political commitment, new thinking, and collaboration between scientists, donors, industry and advocates in both industrial and developing countries.

This report lays out the case for Microbicides and how Europe must act to close the gap between possibility and realization. It invites European policy makers, NGO's and citizens to take up the challenge posed by my Ugandan colleague over a decade ago. A safe and effective microbicide would provide an important tool in the battle to control HIV and STDs in Europe. And it would save innumerable lives in the developing world.

Fortunately, there are positive signs that a groundswell of determination and momentum may be occurring at long last.

- The Irish Government through Ireland Aid has committed €6 million over the next three years to The International Partnership for Microbicides.
- The UK Department for International Development (Dfid) recently gave £16 million to a consortium of UK and African institutions to pursue microbicide development and testing.
- When asked by Newsweek magazine about her aspirations for global health, Melinda Gates of the Bill and Melinda Gates Foundation observed, "During the next decade I'm hopeful that an effective microbicide will be produced and inexpensively delivered to put the power of stopping AIDS into the hands of women."
- Political leaders at the highest levels are finally seeing and understanding for themselves the devastating toll of AIDS in Africa and its global implications, "Microbicides offer a real possibility for helping women protect themselves from HIV/AIDS and other STIs. We need to invest far more resources and energy if we are to make this possibility a reality"
Peter Piot, Executive Director.(UNAIDS)

Conditions are ripe for microbicides to take hold in the public consciousness but to do so will require a significant infusion of capital, strategic vision, and dogged determination. I invite you to add your voices to this growing struggle.

We can no longer afford to keep quiet.

Lori Heise
Director
Global Campaign for Microbicides

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Microbicides: the case for Europe

Contents

Executive Summary	2
The Global Picture	4
The Global Impact	5
The Regional and National Picture	6
The Regional and National Impact	7
Prevention is the Key	8
Microbicides and How They Work	10
The Potential for Microbicides	12
Recent Progress and Developments	14
Outstanding Constraints and Priorities for Action	16
References	19
Appendix	
Microbicides: your Questions Answered	20

Executive Summary

Twenty years after the emergence of HIV, AIDS now accounts for more deaths worldwide than any other infectious disease. The world is watching a pandemic that has seen more than 60 million people infected with HIV/AIDS, unleashing unprecedented social and economic devastation: wiping out important development gains made in previous decades and impeding economic growth in many developing countries.

In many parts of the industrialised world the demographic profile of HIV/AIDS is changing, with more women affected than before. The EU is now being challenged by the spread of HIV among heterosexuals, affecting mainly women, where previously the main affected populations were gay men and injecting drug users. Coupled with this, the epicenters of the AIDS epidemic are also shifting from sub-Saharan Africa and parts of Asia to Eastern Europe where HIV infection rates are rising faster than anywhere else in the world.

Migration and population mobility are now recognised as key drivers of the spread of HIV globally. The EU is no exception. Within the EU those most at risk of the heterosexual transmission of HIV are largely recent immigrants from areas where HIV/AIDS is endemic. Preventing HIV among these hard-to-reach populations is, and will continue to be, a major challenge.

Other sexually transmitted infections (STIs) typically receive less attention than HIV even though they can lead to illness and long-term complications with significant health costs. With an estimated 340 million new cases of STIs each year globally, they are an important public health concern in their own right. But they are also implicated in the spread of HIV, as untreated STIs increase the likelihood of HIV transmission.

Vulnerability to HIV and other STIs is often highest among women, which is partly due to anatomy but mostly due to gender inequalities. In many contexts women are unable to have an equal say in decisions about sex. Often they can not influence the decision to have sex in the first place, let alone protect themselves from HIV and other STIs because they have to rely on the compliance of their male partners to use condoms. If women want to conceive and they suspect that there is a risk of HIV or other STIs, they must make a stark choice between having children and exposing themselves to infection.

Microbicides would revolutionise prevention options for HIV and other STIs. Microbicides are products that women could apply before sex, with or without their partner's knowledge, which would offer protection against HIV and other STIs. Microbicides have been in development for the past decade and there are currently about 60 products, many of them non-contraceptive, in various stages of laboratory and human trials. Experts predict that with adequate investment a first generation microbicide could be available by 2007.

A first generation microbicide, like many other prevention technologies in the past, is likely to be only partially effective. Despite this, it has been estimated in epidemiological models that a first generation microbicide could avert 2.5 million HIV infections worldwide over three years. Averting HIV infections means averting the staggering costs associated with treatment and care and the longer term losses in productivity and economic growth.

The market for microbicides is promising, with detailed analysis estimating the potential market size for a first generation product at US\$ 900 million by 2011, and double this, US\$ 1.8 billion, by 2020 for a third generation product. Demand among women for microbicides is also encouraging with 25 per cent of urban women surveyed in France expressing a strong interest in using a first generation microbicide. Demand among women surveyed in developing countries is even higher.

Scientific advances have seen more microbicides move from the laboratory to the field, with 11 products now in human trials and one entering the final stage of testing. Other advances include studies, in developing and industrialised countries, exploring the key issues around the acceptability of microbicides to women. While there are differences among women in terms of preferred formulation, cost or distribution channel, proven effectiveness of a microbicide against HIV and other STIs is paramount for acceptance by women wherever they live.

The microbicide field is gaining momentum. Key initiatives include: the International Working Group on Microbicides, first convened in 1994, to co-ordinate the microbicide agenda; the Alliance for Microbicide Development, a group that serves the needs of microbicide developers; and the Global Campaign for Microbicides, which draws together the advocacy effort worldwide. The Microbicide Initiative, funded by the Rockefeller Foundation in 2001, brought together five expert Working Groups to report on the scientific, economic, public health, access and advocacy dimensions of making microbicides a reality. These and other initiatives have led to the establishment in May 2002 of the International Partnership for Microbicides, a new public-private partnership, with pledges to date of US\$30 million over three years.

Significant progress has been made without the involvement of major pharmaceutical companies who have not actively invested in microbicide research, mainly due to a perception that the market potential for microbicides in the developed world, a critical for-profit market, is limited.

Public and donor investment has brought microbicides this far, but it falls well short of optimal progress. There is an urgent need to accelerate the development of products already in the pipeline to prove the effectiveness of a microbicide in reducing the transmission of HIV and other STIs in a large-scale human trial. Public and donor funding needs to expand to the investment needed, estimated by the Pharmaco-Economics Working Group at US\$775 million over the next five years, to bring a first generation microbicide to market.

Preparations need to be made now for microbicides access and use. Many of the women who are most vulnerable to HIV and other STIs live in the developing world or in social disadvantage in the industrialised world. A commitment to access is not enough: research is needed to identify and minimise the specific barriers for women. This in turn can inform education and marketing strategies to deliver access to microbicides to the women that need them.

A sustained advocacy effort is necessary to further the scientific and research agenda for microbicides, to facilitate changes in public policy needed to reduce research and development costs and to harmonise regulatory and licensing requirements.

In a global context the major impacts of HIV/AIDS and other STIs are still to come. The scale of the devastation means that no potential avenue should be ignored. In the EU context microbicides offer an important tool to assist in the response to a growing heterosexual HIV/AIDS epidemic and to reduce the burden of STIs among women in general, while giving the increasing numbers of women already living with HIV in the EU a realistic alternative to protect themselves and their partners. For the EU microbicides make good public health and economic sense.

Microbicides are not the solution to the global AIDS crisis but they are the focus of an ambitious yet feasible agenda, rigorously analysed and outlined in the reports of the five expert working groups convened by the Rockefeller Foundation, which has now been taken up by the International Partnership for Microbicides and others in the field.

The Global Picture

Two decades after the emergence of HIV there are more than 40 million people living with HIV/AIDS worldwide, exceeding even the worst-case projections of ten years ago. AIDS now kills more people than any other infectious disease and is the fourth largest cause of death in the world today².

Adults and children infected with HIV since the pandemic began	60 million
Adults newly infected with HIV in 2001	4.2 million
Children newly infected with HIV in 2001	800,00
AIDS deaths, adults and children, in 2001	3 million
Children orphaned by AIDS, and living, end 2001	14 million

Source: UNAIDS¹

HIV is primarily transmitted through unprotected sex, with nine out of every 10 people with HIV living in developing countries¹. Women are increasingly affected by HIV/AIDS, representing 47 per cent of those infected globally, and more than 55 per cent of those infected in sub-Saharan Africa¹. Increased HIV infection among women creates a dynamic in family and community networks where the primary caregivers are themselves in need of care. Even in industrialised countries such as the USA, where the early epidemic was largely among gay men, women now account for 31 per cent of all new HIV infections².

In the early eighties the HIV epidemic was largely driven by epicenters in Africa and major cities in the industrialised world, followed by epicenters in South East Asia and Latin America in the early nineties. Today, HIV infection rates are rising faster in Eastern Europe than anywhere else in the world².

Migration and population mobility has emerged as a key phenomenon underpinning the AIDS pandemic^{3,4}. Mobility associated with trade or labour, humanitarian or natural disasters, war or conflict, temporary or permanent migration and even tourism have all been implicated in the spread of HIV within countries and across borders.

The global spread of other sexually transmitted infections (STIs) has continued unabated alongside the HIV epidemic. Other STIs often receive less attention than HIV even though they lead to morbidity on a huge scale. The World Health Organisation (WHO) estimates that there were 340 million new cases of four major curable STIs in 1999⁵. Globally the highest rates of STIs are generally seen in urban men and women in their most sexually active years, with women on average becoming infected at a younger age. The prevalence and incidence of other STIs varies across the globe with higher rates usually found in developing countries. As with HIV, there has been an alarming increase in cases of gonorrhoea and syphilis in Eastern Europe in the past decade⁵.

While there are more than 20 bacterial or viral pathogens transmissible through sexual intercourse, most are curable. However, the spread of curable STIs continues in spite of the availability of treatment as many STIs are asymptomatic, especially in women, and can only be detected by accessing specialist sexual health screening.

The Global Impact

The impact of HIV/AIDS is unprecedented. Not since the Black Death devastated medieval Europe has the world witnessed so many deaths from an infectious disease. HIV/AIDS has moved from being a major public health concern to become a key issue for economic and social development, critical to a variety of policy areas outside of health. Such is the destruction and destabilisation being caused by AIDS that it is now also regarded as a global security issue⁶.

HIV/AIDS reverses development because it erodes some of the key determinants of economic growth. A recent landmark study by the World Bank into the empirical relationship between economic growth and AIDS in 80 developing countries found that the epidemic substantially reduced the rate of Gross Domestic Product growth, when controlling for other variables⁷. This in turn has exacerbated poverty, which leads to increased vulnerability to HIV infection. Even in the industrialised world where the impact of HIV is less visible, AIDS leads to death or chronic illness typically among the most productive people in society: the young and middle-aged.

In many countries HIV/AIDS is reversing key health gains: decreasing life expectancy; lowering productivity due to increased morbidity and mortality among the workforce; and generating significant public sector costs, especially in industrialised countries where publicly funded treatment and care is available.

Vulnerability to HIV is often highest among women. This is partly due to anatomy but mostly due social, cultural, and economic inequality. In many contexts women are socially excluded from taking an equal part in decisions relating to sex with men and from the information and services which provide the means to protect themselves. More broadly, women may lack the economic independence to make the choices they want to make in relation to their sexual health.

Other STIs are a major public health concern. Both symptomatic and asymptomatic infection can lead to serious medical complications, including chronic disease and infertility, especially among women and result in long term consequences for individuals and communities. In addition, the presence of other STIs in men or women can enhance the sexual transmission of HIV by a factor of up to 10⁵. In developing countries other STIs are amongst the top five disease categories for adults seeking health care; in women of childbearing age, other STIs are second only to maternal factors as causes of disease and death⁵.

New cases of selected curable Sexually Transmitted Infections (STIs) among adults in 1999 worldwide

Syphilis	12 million
Gonorrhoea	62 million
Chlamydia	92 million
Trichomoniasis	174 million
Global Total	340 million

Source: WHO⁵

In the international arena, the EU and its member states are key stakeholders in efforts to promote global economic and social development, which in many countries implies taking an active role in responding to HIV and other STIs in countries already devastated by HIV, or attempting to control HIV and other STIs before they take hold in the population. With each passing decade a growing number of countries in all regions of the world have had to prioritise HIV and other STIs to avoid a development catastrophe within their borders.

The Regional and National Picture

As of the end of 2001, 550, 000 people were estimated to be living with HIV/AIDS in Western Europe¹. The total numbers of cases of AIDS and deaths from AIDS-related illnesses have declined rapidly since 1996 with the introduction of highly active antiretroviral therapy for HIV. However, AIDS cases attributed to heterosexual contact have been rising in the EU, surpassing AIDS cases among gay men and injecting drug users for the first time in 2001⁸.

In 2001 there were 12, 000 HIV diagnoses⁸ in the EU. Importantly, this figure does not include three member states seriously affected by HIV - France, Italy, and Spain - as HIV cases are not reported at a national level. While the overall number of newly diagnosed HIV infections shows no consistent upward trend, changes within new cases of HIV give cause for comment.

Heterosexual transmission of HIV has increased sharply in the EU while new cases among injecting drug users and gay men remain largely stable⁸. Each year since 1999 new cases of HIV attributed to heterosexual contact have been the most common route of HIV transmission reported in the EU⁸. In Ireland, heterosexual transmission has been the most common exposure category for new cases of HIV since 1997 and accounted for almost two-thirds of new cases of HIV in 2001, outnumbering cases among injecting drug users and gay men combined⁹.

In the non-EU countries of Europe there have been some alarming increases in HIV. In Eastern Europe since the mid-nineties HIV infection rates have been spiraling upwards in Estonia, Latvia, Russia and the Ukraine, largely driven by injecting drug use and heterosexual transmission⁸.

New cases of selected curable Sexually Transmitted Infections (STIs) among adults in 1999 in Western Europe*

Syphilis	0.15 million
Gonorrhoea	1 million
Chlamydia	5 million
Trichomoniasis	11 million
Total	17.2 million

Source: WHO⁵

WHO estimates that there were over 17 million new cases of four major STIs in 1999 in the Western European region⁵. The prevalence of Chlamydia, a leading cause of pelvic inflammatory disease and one of the most common STIs, amongst pregnant women in Europe ranges from just under 3 per cent in Italy to 8 per cent in Iceland⁵.

In Ireland there are fourteen notifiable STIs in public health surveillance. Annual trends document an increase of 85 per cent of cases of STIs in Ireland between 1995 and 2000, and a tripling of reported cases since 1989¹⁰. The four major STIs monitored by WHO are also showing an upward trend here.

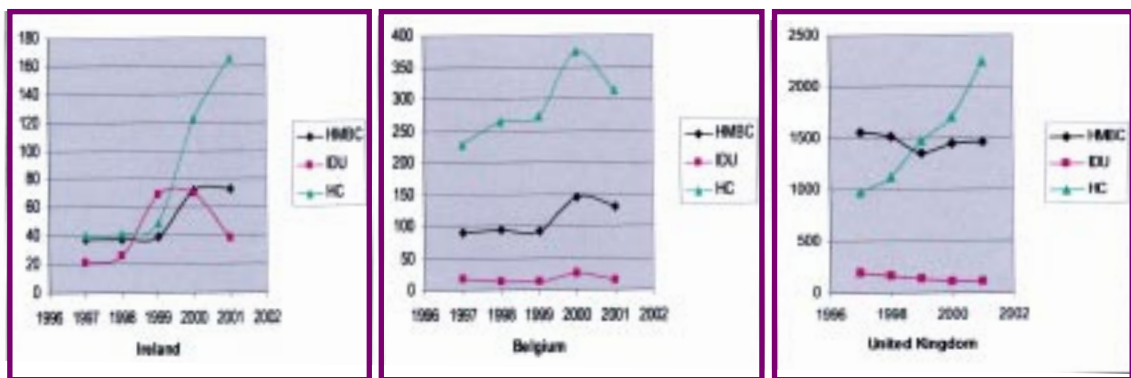
* Western Europe here includes non-EU countries: Albania, Iceland, Norway, Malta, Slovenia, Switzerland, TFYR Macedonia and Yugoslavia.

The Regional and National Impact

A corollary of the rise in heterosexual cases of HIV and AIDS is the increased number of women living with HIV/AIDS in the EU, with women making up almost 50 per cent of new cases of HIV in 2001⁶. This has implications for HIV/AIDS prevention policy in the region, which has until now been largely developing capacity to control HIV among gay men and injecting drug users. While awareness of HIV/AIDS may be high among women in general, awareness amongst women who are most at risk of HIV may be inadequate. This poses serious challenges to mounting an effective response to the increasing impact of HIV on women within the EU.

Migration and mobility issues are now recognised as a key undercurrent of HIV/AIDS in the EU^{4,6}. Since the late eighties a growing proportion of heterosexual cases of HIV in the UK (72 per cent in 2001) have been among people from countries where there are generalised[†] epidemics, the majority of whom are women⁶. A similar pattern is now apparent in many other member states, including Ireland, and anecdotally in France, Italy and Spain where data is not available. Immigrants and other mobile populations tend to have poorer access to health services leading to later presentation to diagnose and treat their HIV infection. This in turn, exacerbates their vulnerability to HIV. Since 2001, ethnicity data is being collected with HIV and AIDS notifications across Europe to allow for improved monitoring of mobility trends and improved targeting of affected communities⁴.

Figure 1 Trends in newly acquired HIV infection by transmission group (1997-2001)



Source: EuroHIV⁶

HIV infection leads to significant public sector costs in the EU. It has been estimated that the average lifetime medical costs for treating one HIV infection is US\$200,000¹¹. Although it can be argued that the economic impact of HIV/AIDS in the EU is less catastrophic than in many regions of the developing world, there is nevertheless a major impact in terms of deaths, hospitalisations and treatment for HIV, and loss of productivity through chronic illness.

Other STIs continue to have a major, if less quantifiable impact. While most STIs, including syphilis and gonorrhoea, have decreased in most EU member states, chlamydia rates remain static and common⁵. The costs in terms of diagnosis, care, and treatment are significant because of the millions of cases of STIs requiring treatment each year. The costs of untreated STIs are likely to be even higher given the chronic medical complications that they can cause, especially among women. As there is no ethnicity data collected for other STIs it is not possible to assess any mobility trends in the EU at this time. However, in the past decade there has been more than a ten-fold increase in cases of syphilis in many states of the former Soviet Union, coupled with significant increases in gonorrhoea in countries including Estonia, Russia and Belarus⁵.

The major global impacts of HIV and other STIs are yet to come. In the EU, for the first time we are

[†] A generalised epidemic is where screening among pregnant women consistently shows a HIV prevalence rate of > 1 per cent

faced with a heterosexual outbreak of HIV, affecting mainly people from countries where HIV is widespread, while also mindful of the potential for the explosive spread of HIV and other STIs occurring in Eastern Europe, including some EU accession countries, to have a major impact in the EU of the future.

Prevention is the Key

Two decades after the advent of HIV, drawing on a wealth of collective experience from around the globe, we know that it is possible to contain the spread of HIV and other STIs. In developing countries such as Senegal, Uganda, and Thailand, major prevention programmes which integrate education, prevention, care and support have delivered substantial reductions in the spread of HIV and other STIs¹. Elsewhere effective responses have curbed epidemics among sub-cultures including gay men, injecting drug users and sex workers in various parts of the industrialised and developing world. Successes in prevention have been firmly rooted in communities, with the active participation of people living with HIV/AIDS, and have required significant political will, investment and social mobilisation for their implementation.

Successes in prevention have also recognised and responded to the pervasiveness of denial, stigma, discrimination and secrecy around HIV/AIDS and other STIs. Prevention which assists individuals and communities to counter denial, stigma, discrimination and secrecy, whilst protecting human rights, is consistent with good public health practice¹⁴.

Prevention has included efforts to stem all the potential routes of HIV transmission: perinatally from mother to child; in blood-to-blood contact through unsterile injecting practices or through infected blood products; and through the most common route of transmission, unprotected sex. Central to these efforts has been timely promotion of a variety of prevention technologies to reduce the risk of sexual transmission of HIV and other STIs.

Current HIV/STI Prevention Technology

The male condom is the most familiar technology associated with HIV and synonymous with the notion of safe sex, a measure of the impact of extensive social marketing that has permeated the global culture of the past 20 years. The male latex condom is affordable, accessible, and up to 95 per cent effective in the prevention of HIV. It offers protection against many other STIs and is relatively easy to use. Despite this there are significant cultural and social barriers to the consistent use of condoms, not least because it is male-controlled. In many contexts women are unable to protect themselves, even if they are aware of a HIV risk, because they are not in a position to request their male partners use condoms. If women want to conceive, they have no affordable alternatives to ensure safety from HIV and other STIs.

Less well-known, the female condom was approved by the US Food and Drug Administration for single use to prevent pregnancy and STIs in 1993¹². Since then there have been small-scale trials to introduce the device into various sub-populations. Currently one type of female condom made of polyurethane is on the market. It is inserted prior to sex, and unlike some other contraceptive barrier methods, requires no fitting. It is available without prescription and the fact that it is female-controlled is one of its key strengths but there are also a number of limitations. While studies have found the device to be acceptable to women, in practice using the device requires a male partner's knowledge (and possibly his consent), which may contribute to inconsistent use in various settings¹². In addition, the female condom costs more than 10 times as much as a male condom¹², which means that it is often out of the reach of the women who need it most. Despite these limitations, large-scale introductions are now being attempted¹² in some 15 developing countries¹².

Efficacy and Consistency

Protection from HIV or other STIs is a function of how good a method is at preventing infection at each act of sexual intercourse (efficacy) and how consistently it is used.

A 95 per cent efficacious method (a male condom) used in 20 per cent of sexual contacts provides less protection than a 60 per cent efficacious method used in 40 per cent of sexual contacts¹³.

Treatment of other STIs has been found to reduce the rate of transmission of HIV by up to 40 per cent in the general population⁵. Consequently, promoting access to affordable treatment for STIs is seen as a priority in many HIV prevention programmes.

Implementing this priority can be a challenge, as many people with STIs are asymptomatic and also because of the strong cultural taboos which surround people seeking treatment for a STI, even if they know they are infected. Despite this there have been successes with, for example, outreach programmes to female sex workers enhancing their access to sexual health screening which in turn reduces rates of STIs among their clients, and consequently the general population.

Voluntary HIV testing, especially when carried out with adequate pre and post-test counselling, is also an important tool in HIV prevention. With HIV typically asymptomatic for between 7 and 10 years, people who test positive can benefit from early clinical intervention and protect their partners from infection. Pregnant women with HIV can be offered antiretroviral therapy which can almost eliminate the risk of transmission from mother to child. People who test negative can explore risk-taking practices in pre and post-test counseling and modify their behaviours to reduce their vulnerability to HIV.

In contrast, mandatory HIV testing is proposed at times in an effort to combat HIV among certain sub-populations, such as immigrants. However, it is neither feasible nor desirable to force people to be tested and retested throughout their lives¹⁴. For example, it would only be feasible to screen longer-term permanent migrants, thus all other population flows created by conflict, trade or tourism can still drive the movement of HIV. Equally it is a potentially costly exercise and, because it would be unlikely to include any counseling it is unlikely to deliver any behaviour change¹⁴. Approaches which target mobile people such as refugees, business travellers, skilled workers or tourists and alert them to their vulnerability to HIV can deliver on-going benefits in sustained behaviour change and in access to voluntary sexual health screening.

Other strategies often promoted as part of the HIV prevention have focused on partner reduction and monogamy. While promotion of these methods generally receives broad support in most communities, partner reduction alone is not a fail-safe HIV and other STI prevention strategy. In particular, gender based social norms can lead men to seek multiple partners. Even when women have only one partner, they can be at risk through that partner's other sexual relationships.

Current HIV and other STI prevention technologies although successful up to a point when consistently accessed and used, cannot ultimately win the fight against HIV and other STIs. Until now women have had to rely largely on the compliance of their male partners to protect themselves. And that is still the case today. But over the past decade there has been a growing field of research to develop microbicides, a female-controlled prevention technology that could radically alter the landscape of protection against HIV and other STIs in the near future.

Microbicides and How They Work

A microbicide is a compound that women can use vaginally to protect themselves against HIV and other STIs. A microbicide could be produced as a gel, cream, suppository, or in the form of a ring or sponge that slowly releases the active ingredient over time. It could be in a contraceptive or a non-contraceptive form. Today, there are over 60 microbicides ready for further stages of testing in laboratories and clinics around the world, but none are available yet because the research is severely under-funded^{2,13,15}. With strong investment and political will, experts project that a safe and effective topical microbicide could be on the market by 2007^{2,13}.

An effective microbicide needs to interrupt the complex sequence of events between exposure to HIV (or other STI pathogen) in sexual intercourse and the establishment of infection. The microbicides currently in development have four main modes of action and offer protection by:

- * killing or inactivating HIV or other pathogen
- * fortifying normal vaginal defenses
- * preventing viral access, attachment, fusion or entry to certain cells in the vaginal mucosal tissue; and
- * preventing viral or other pathogen replication^{2,13,15}

HIV is a viral infection. Of the 20 or so pathogens which can be transmitted sexually, most are viral or bacterial. Many of the microbicides currently awaiting further development offer partial protection against HIV and a number of STIs^{2,13,15}. Full protection against HIV and other STIs is likely to be achieved only through the combined use of several microbicides.

The Ideal Microbicide would be:

Effective against HIV and other STIs

Active as it is inserted, and for a few hours after

Safe

Inexpensive

Available without prescription

Colourless, odourless, tasteless, invisible

Stable and easy to store

Pleasure enhancing

Available in contraceptive and non-contraceptive forms^{2,13,15}

There may never be one ideal microbicide. Market research has shown that even if a messy, unpleasant product were available, women would use it if it were proven to be effective against HIV^{2,13,15}. Therefore, the immediate priority is to develop a microbicide that is proven to be effective against HIV which can be used consistently by women who need it most.

It can typically take about 10 years for a product lead, such as a treatment, to go through the required testing phases and be registered and approved for use. Getting a microbicide to market takes even longer because evaluating a new prevention technology—as opposed to a new treatment—typically requires larger, more complicated clinical trials. This clinical research needs to be complemented and informed by research into the acceptability of the new technology, including preferred formulations and cost, followed by regulatory and approval processes.

Before a product lead enters human testing it must first go through a series of pre-clinical tests in both the laboratory and in animals. Once there is preliminary evidence of activity and safety, a product can proceed onto clinical trials in humans. The first set of trials, known as Phase I trials, are designed to establish in a small number of volunteers, whether the product lead being tested appears safe for human use. Eventually, these safety trials are expanded to include a wider array of individuals, including those who may also have other sexually transmitted infections, including HIV (Phase II). Eventually, if successful, product leads go on to large scale, Phase III trials to evaluate their effectiveness and longer-term safety.

One candidate microbicide, Carraguard™, is about to enter a Phase III trial in 2002 with 6, 000 women enrolled in multiple sites in South Africa and Botswana¹⁶. In this trial, women will be randomised to receive condom counseling and the experimental microbicide or condom counseling and a placebo microbicide (without the active ingredient). Effectiveness will be demonstrated if there are statistically fewer new HIV and STI infections among the women receiving the active microbicide compared to those using the placebo.

A first generation microbicide, like many other prevention technologies in the past, is likely to be only partially effective. Experts predict that a first generation microbicide could be 50-60 per cent effective against HIV¹⁷. This would mean that a first generation microbicide would be promoted to be used as an adjunct to condom use or as a back up if condom use were not possible. Subsequent generations of microbicides may be more effective and could be used as stand alone protection.

In 1955 the first generation polio vaccine introduced by Jonas Salk was only 60 per cent effective. By the time an improved vaccine was introduced six years later, the partially effective Salk vaccine had virtually eliminated polio in the United States, driving down the number of new infections by 95 per cent¹³

Even if a candidate microbicide is shown to be safe and effective in clinical trials it must also be acceptable and accessible to end users: women wanting to protect themselves and their partners from HIV and other STIs. For a microbicide to be used consistently, women must understand the benefits, the elements of correct use, and the potential side effects. Social and market research can shed light on the characteristics that are most likely to support women's willingness and ability to use a microbicide consistently as well as men's attitudes to their partners microbicide use. The way the product is positioned in the market, the cost to women, and the distribution points most conducive to widespread use are also critical to the successful introduction of a new prevention technology.

Regulatory and approval processes will need to allow for the rapid introduction of microbicides in developing countries, where they are urgently needed. Typically it takes about 10 years for a product approved for use in the developed world to reach developing countries¹⁸. With an effective HIV prevention technology this delay would be catastrophic for the millions at-risk individuals who are waiting for the new technology to 'trickle down'.

The Potential for Microbicides

The global potential of microbicides has been an educated guess-until now. The London School of Hygiene and Tropical Medicine has used epidemiological modeling to calculate the impact that a 60 per cent effective microbicide could have in controlling the spread of HIV in 73 low-income countries.

Assuming conservatively that 20 per cent of individuals who are currently in contact with services use a microbicide in 50 percent of occasions that they do not use condoms, a 60 per cent effective microbicide could avert 2.5 million HIV infections over three years^{2,15}. If the product was used by 30 per cent of individuals already reached by services then it could avert 3.7 million infections over three years in the developing world^{2,15}.

Averting HIV infections means averting the staggering costs associated with HIV infection. UNAIDS projects that US\$4.4 billion will be required in direct HIV/AIDS treatment and care costs alone each year over the next three years worldwide¹. Were microbicides to avert 2.5 million HIV infections globally between 2002 and 2005 an estimated US\$2.7 billion would be saved in health care costs, with a further productivity benefit of US\$1 billion in the same period².

The cost effectiveness of preventing HIV is affected by the cost of the intervention and the number of new infections averted¹⁹. Societal prevention interventions, like male condoms (and potentially microbicides), have been shown to be highly cost effective because they can inexpensively reach large numbers of at-risk individuals¹⁹.

The Pharmaco-Economics Working Group of The Microbicide Initiative has carried out a detailed analysis of the market potential of first, second and third generation microbicides in the developing and industrialised world. Assuming that less than 10 per cent of sexually active women will use the products, a first generation product could have a market size of US\$900 million by 2011, and a third generation product could have sales of US\$1.8 billion by 2020². These are conservative estimates. If microbicides were able to meet a broader set of needs for women, such as a general vaginal hygiene product, then the optimistic peak-market size could be \$US5 billion².

Table 1. Summary of microbicide market evolution scenarios

	1st Generation	2nd Generation	3rd Generation
Expected Launch	2007	2012	2017
Formulation	Vaginal Only	Vaginal & Rectal	Vaginal & Rectal
Indications	HIV, possibly other STI's possibly other contraceptive	HIV, herpes, gonorrhoea, HPV, Chlamydia; choice of contraceptive or non-contraceptive	HIV, herpes, gonorrhoea, HPV, Chlamydia; choice of contraceptive or non-contraceptive
HIV Effectiveness	50% - 60%	70% - 90%	85% - 97%
Contraceptive Effectiveness	75%-85%	80%-90%	90%-97%
Use Instructions	W/condom or device	Stand Alone	Stand Alone
Sales Channel			
Industrialised Countries	Prescription Only	Over the Counter	Over the Counter
Developing Countries	Over the Counter	Over the Counter	Over the Counter

Source: *The Microbicide Initiative*²

Demand for microbicides among women, including married women at risk because they or their partners have other partners, is encouraging. The EU HIV/AIDS Programme in Developing Countries commissioned market research in 11 countries to gauge the overall demand for a microbicide-like product. The research found that 25 per cent of urban women surveyed in France were 'very interested' in a first generation microbicide that offered additional protection when used with male condoms, priced at twice the local cost of male condoms¹². The Pharmaco-Economics Working Group of The Microbicide Initiative used sophisticated modeling to extrapolate the EU market research to other countries and concluded that even at five times the cost of the male condom, almost 30 per cent of women in the UK would be 'very interested' in a microbicide¹⁷. In developing countries, such as the Ivory Coast and Kenya, more than 50 per cent of women would want to use a microbicide even if it cost five times as much as a male condom.

In the EU and Irish context microbicides would offer a technology which could be promoted to those women at greatest risk of the sexual transmission of HIV. Based on HIV/AIDS surveillance data over the last five years, a key target group would be married women from countries with a generalised HIV epidemic. Within the EU these women are mainly from African, Asian and Caribbean backgrounds where reproductive health is culturally seen as a woman's role. This makes promoting a female-controlled prevention technology, microbicides, a more culturally accessible and culturally appropriate response to HIV - especially when compared to male condoms. Equally, women wanting to have children could choose a non-contraceptive microbicide to offer partial protection against HIV and other STIs.

Women living with HIV would also be a key target group for microbicides, giving them protection against other STIs which can pose an even greater health risk to people whose immune system is compromised. As microbicides are likely to protect both partners they would also give HIV-positive women a technology which they control to share the responsibility of safer sex.

Microbicides could also help to reduce the burden of other STIs in the EU, estimated by WHO at 17 million new cases each year for four major curable STIs⁵. In addition to averting the public and private costs of diagnosis and treatment of STIs, there would also be a reduction in the long-term complications which result from untreated STIs such as cervical cancer, pelvic inflammatory disease and infertility. A key market segment for microbicides would be women from the general population, especially young women, where STIs such as chlamydia are very common. In the US, 40 per cent of all reported cases of chlamydia are young people between 15 and 19 years old: over one young woman in 10 is infected²⁰.

Microbicides stand at the intersection of three movements: sexual and reproductive health, HIV/AIDS and women's health, movements which have significant existing infrastructure and capacity which can be mobilised to reach various market segments and distribute microbicides to women in the EU that need them most.

In an international context, microbicides could be part of the EU's effort to bring about economic and social development in the developing world. Indeed, the EU has already begun to tap this potential and has been part of efforts to date to put microbicides center-stage on international development policy agendas.

Microbicides are technologically feasible and offer the potential to provide women globally with the means to protect themselves, and their sexual partners, from HIV and other STIs, thus averting millions of infections and the ensuing economic and social costs. At an EU level microbicides would have a substantial market size among women in the general population but could also be invaluable to prevent the spread of HIV and other STIs among women from ethnic minority backgrounds, young women, and HIV-positive women. The sexual partners of women using microbicides are also likely to benefit. Existing infrastructure in HIV/AIDS, reproductive and women's health could be tapped to promote access to microbicides by women.

Recent Progress and Developments

Scientific Gains

The past decade has seen many candidate microbicides move from the laboratory to the field. In 1994 there were only 12 products in pre-clinical evaluation stages and few products had entered clinical trials²¹. Today there are 45 products in pre-clinical evaluation and 11 products in clinical trials^{2,13}. This progress, with severely limited resources, is all the more significant when one considers that no major pharmaceutical company is actively involved in microbicide research and development. If adequate resources, comparable to that of a large pharmaceutical company, were invested into research and development then a first generation microbicide could be on the market by 2007^{2,13}.

Fig. 2 Microbicides in Clinical (Human) Trials, Winter 2002

			Carraguard tm
		BufferGel tm	
		Pro-2000	
	Lactin Vaginal Capsule		
	Emmelle tm		
Acidform tm			
Invisible Condom tm			
Savvy tm			
Cellulose Sulfate			
Polystyrene Sulfonate			
PMPA			
	Phase I	Phase II	Phase II/III
			Phase III

Source: Alliance for Microbicide Development, 2002 cited in the Global Campaign for Microbicides¹³

Briefly, the three most advanced candidate microbicides in clinical trials are^{2,13,15}

- *Carraguardtm* made from carrageenan, an inexpensive substance derived from seaweed that is widely used as an additive to foods and cosmetics. *Carraguardtm* is a fusion inhibitor, which works to prevent HIV cells from fusing with target cells in the vagina. Trials indicate that it is a non-contraceptive.
- *BufferGeltm* keeps the vagina acidic even during intercourse and creates a physical barrier that inhibits the passage of pathogens into the vaginal and cervical epithelium.
- *Pro-2000* contains a synthetic polymer that binds to the HIV virus, thereby disrupting binding of the virus to target cells. The gel probably works in a similar fashion to block chlamydia and herpes simplex virus infections.

Policy and Research

Considerable acceptability research has been carried out in different settings to determine the product characteristics most conducive to the consistent use of microbicides by women around the globe. While there are differences in preferences for the formulation of microbicides, proven safety and effectiveness against HIV and other STIs is paramount for acceptance by women wherever they live. Surveys among men, in the US, Mexico and Zimbabwe, have also indicated support for their female partners using microbicides^{2,13}.

Market research has been commissioned to determine the demand by women and potential market size. A recent study by the Alan Guttmacher Institute estimated that 12.7 million American women would be 'interested', and 7.7 million would be 'very interested' in using a microbicide^{2,13}.

Complementing this work, a survey by the UK Medical Research Council in 1995 and an independent follow-up survey in 1999 explored the obstacles for major pharmaceutical companies to invest in microbicides. While there was a better environment for industry to invest in the 1999 survey, critical barriers include the proof of concept and a perception that the market potential in the developed world, a critical for-profit market, is limited^{2,13}.

The policy agenda has focused significant attention to the cost of microbicides to users. Microbicides must be available and accessible to the women who need them most. Like the male and female condom, the unit price is extremely critical because microbicides are intended to be used with every sexual contact. With many of the women who need microbicides living in a developing country or living in socio-economic disadvantage in the industrialised world, cost is integral to consistent use. Costs can be picked up at all stages of development in pre-clinical and clinical trials, regulation, marketing, production and distribution of the product and consequently must be considered at all stages of the research and development pathway.

“Microbicides offer a real possibility for helping women protect themselves from HIV/AIDS and other STIs. We need to invest far more resources and energy if we are to make this possibility a reality”

Peter Piot, Executive Director.

Joint United Nations Global Programme on AIDS (UNAIDS)¹⁵

Coordination and Collaboration

The global movement to mobilise around microbicides is gaining momentum. Sustained efforts have been made through symposia, conferences, international working groups and other fora, to galvanise support for microbicides among scientists, donor and international agencies, and government and non-government organisations. Mechanisms have been set up to allow for speedier dissemination of research and policy advances to interested stakeholders, including key decision-makers.

Key initiatives include: the International Working Group on Microbicides, first convened in 1994; the Alliance for Microbicide Development founded in 1998, which facilitates collaboration of the scientific enquiry in microbicide development; the Global Campaign for Microbicides, launched in 1998, which draws together the advocacy effort among non-government organisations worldwide; and The Microbicide Initiative funded by the Rockefeller Foundation which convened five working groups to develop a road map for taking the field forward. In 2002 these expert working groups published five key papers, a scientific blueprint a, pharmaco-economics study, an analysis of public health impact, an access agenda, and a global plan for microbicide advocacy.

At an EU level, International Family Health, a UK-based non-government organisation has been funded to expand microbicide advocacy in Europe in 2002. Among member states, the UK Department of International Development has recently announced a £16 million investment over five years²². Ireland Aid has pledged €6 million over three years. These and other initiatives have helped to bring the economic and public health case for investing in microbicides to the attention of international, regional and national stakeholders.

Looking to the future, the establishment in May 2002 of The International Partnership for Microbicides (IPM), a new public-private partnership, marks another significant step forward in the path to making microbicides a reality. The five expert reports published by The Microbicide Initiative in 2002 will be the springboard for the development of the priorities of the IPM which has pledged to date of US\$30 million.

Outstanding Constraints and Priorities for Action

Accelerate the Development Pipeline

There are almost 60 product leads in the development pipeline ready for further stages of testing. Public and donor investment has brought us this far but has fallen well short of what is required for optimal progress. There is an urgent need to press ahead with some of the products already in the pipeline to reach proof of concept, a critical barrier to the active involvement of major industry in microbicides. Proof of concept of a prevention technology is more difficult than for a treatment, involving much larger clinical trials and observation of trial participants over months and years. In addition, microbicide trials will be carried out where women are more at risk of HIV and other STIs: in developing countries where women may be marginalised and find it difficult to participate without the consent of a husband, father, or brother.

The small companies and academic research organisations doing almost all of the work in microbicide science lack the capacity for testing, formulation, manufacturing and packaging and need to rely on numerous contractors and sub-contractors. This is costly and time-consuming. Opportunities exist to coordinate investment as a whole and thus save time and money. New understandings of the microbiological mechanisms of HIV and other STI transmission over the past decade have resulted in the discovery of more prospective points to interrupt transmission with a microbicide. This demands an expansion in the area of basic science to exploit these leads and generate additional candidate microbicides into the pipeline.

Expand Public and Donor Funding

Public and donor funding needs to expand to bring a first generation microbicide to market because the profit potential for private investors is not sufficient to propel innovation. The Pharmaco-Economics Working Group has confirmed that the return on investment in a first generation microbicide would be negative—that is, the revenue generated would not cover the costs of development and of capital². A second generation microbicide could get to market without public subsidy because of increased market potential and decreased development costs. Only a third generation product, however, would generate sufficient return, estimated at US\$428 million, for major pharmaceutical industry investment².

The Pharmaco-Economics Working Group has calculated that if all of today's leads were owned and managed by one company, at least US\$775 million would need to be invested over the next five years in direct product development costs to ensure a high likelihood of developing at least one safe and effective microbicide². This calculation does not include the discovery and exploitation of new leads, work on access and product introduction, or the advocacy effort.

Demand for a return on investment leads to a lack of investment by major pharmaceutical companies in technologies for the 'poor'. Microbicide advocates are actively pursuing options in the areas of 'demand pull' and 'technology push' to create supportive environments for a profit motive and to decrease obstacles to investing in research and development. Many of the options being proposed involve changes to public policy to enable a more secure footing for investors, especially industry. Innovative strategies include low interest loans for building manufacturing plants, providing tax credits and incentives, reducing royalty payments, elimination or reduction of tariffs, and allowing access to publicly funded clinical trial sites.

Prepare for Microbicides Access and Use

Research to date has focused largely on issues pertinent to the early stages of product development, including formulations and acceptable costs to users. Increasingly, the research agenda needs to explore product introduction and access issues. Production positioning and marketing will be critical to the uptake of microbicides. If, for example, microbicides are promoted initially to sex workers, other groups of women, such as married women, may reject them. In addition, the distribution mechanisms most likely to deliver low-threshold access to microbicides by women will need to be determined. Implicit in these considerations is whether a first generation microbicide will be available over-the-counter or by prescription. The optimal scenario is that microbicides would be available over-the-counter in developing countries. A commitment to ensuring access by women in the developing and industrialised world is not enough: we will need to identify and minimise the specific barriers. If microbicides are acceptable to women and easy to access, this will contribute to market share and facilitate industry investment in the future.

Education campaigns need to be researched and developed to ensure that women choosing microbicides will know how to use them correctly and know of side effects. Equally, as the arrival of microbicides will be akin to the contraceptive pill, education strategies will need to be devised for various key actors including health and education professionals, and community leaders. As a first generation product will not be 100 per cent effective, these education efforts will need to be sophisticated and present microbicides in a hierarchy of protection options.

*The key education message to women could be:
"Condoms used correctly every time offer the best protection, but in the absence of a condom, a microbicide can help reduce your risk of infection."¹³*

Advocacy

A sustained advocacy effort is necessary to further the scientific and research progress of microbicides and must be adequately resourced. Unlike vaccines, microbicides are an entirely new product category. Advocacy is needed to generate and sustain the interest of the scientific community to apply their expertise to microbicides, to convince public and donor agencies to invest scarce resources, and to provide feedback to stakeholders on progress. Advocacy can work to increase pharmaceutical companies' interest and work to counter the myth that microbicides will only have a market in the developing world. Advocacy can help to structure the research agenda, fostering innovation in the introduction of a new product category including research into the cost effectiveness of microbicides with different markets and sub-populations.

Condoms make safer sex his decision, microbicides will make it yours¹³

Advocacy can look to facilitating advances in public policy to ensure that costs associated with research and development are minimised: putting forward options for debate such as subsidised venture capital, guaranteed purchase mechanisms, revenue-linked tax breaks, and public-private research partnerships. Public policy also needs to be involved in striking the balance between intellectual property and consumers' need for a safe, affordable product. Advocacy can also help to harmonise regulatory approval and licensing requirements. For example, the US Food and Drug Administration (FDA) has recently moved to streamline regulatory processes to fast-track essential prevention technologies such as microbicides. A similar approach could be proposed to the EU at

the European Medicines and Evaluation Agency (EMA). Approval by the FDA and the EMA would speed up approval in other jurisdictions and is essential for many donor agencies, based in the USA and Europe, wishing to purchase and donate in bulk.

Microbicides are at the forefront of a promise for women globally to give them a technology, which they control, to avoid HIV and other STIs and the resulting morbidity and mortality. It is an ambitious agenda with one speaker at a recent conference likening it to the great European cathedrals built in the middle ages by architects, artisans and labourers who never knew if they would see the completed structure. They persisted, so must we.

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Microbicides: Your questions answered

What is a microbicide?

A microbicide is a product (e.g. a gel) that a woman applies before sex that would give protection against HIV and other sexually transmitted infections (STIs). Importantly for women wanting to conceive, many of the microbicides currently in development are non-contraceptive in laboratory trials.

Are microbicides currently available?

While as yet there is no microbicide on the market, there has been an expansion of products in the development pipeline over the past ten years. Much of the research and development of microbicides is severely under funded and no major pharmaceutical company is actively involved at this stage. Despite this, one candidate microbicide is entering the final stages of human trials in late 2002.

Why isn't the pharmaceutical industry involved?

Two studies, in 1995 and 1999, have surveyed major pharmaceutical companies and found that the major barriers to investment in microbicides include a perception that microbicides will have a limited market, and therefore limited profit, in developed countries and that there is still no proof that a microbicide will prevent HIV or other STI transmission. This 'proof' will be forthcoming if final stage human trials currently being planned show a significant reduction in HIV and other STI transmission among trial participants.

What is in the development pipeline?

The microbicides currently in development have various modes of action to interrupt the complex sequence of events which lead to the transmission of HIV and other STIs in the vagina. Carraguard[™], which is entering the final stage of human testing, prevents HIV cells from fusing with target cells in the vagina.

Will the development of microbicides ever see a profit?

The lack of substantial industry investment means that public and donor funding will be needed to bring a first generation microbicide to market. A Pharmaco-Economics Working Group convened by the Rockefeller Foundation has estimated that a second generation microbicide could get to market without public subsidy because of increased market potential and decreased development costs. Only a third generation product, however, would generate sufficient return, estimated at US\$428 million, to attract major pharmaceutical industry investment.

So would microbicides eliminate the need for condoms?

Certainly not. It is estimated that a first generation microbicide could be 50-60 per cent effective against HIV meaning that it would be promoted for use with, or as a back-up to, condoms. Many women and men cannot use condoms in many situations, or cannot negotiate using condoms in many more situations, so microbicides would be an important way to reduce, but not eliminate, the risk of HIV and other STIs, particularly if couples also want to conceive.

Why do we need microbicides if we are going to have a HIV vaccine?

With more than 40 million people living with HIV/AIDS in the world today, and more than 340 million new cases of curable STIs each year, the world needs both a HIV vaccine and microbicides. A HIV vaccine will only protect against HIV whereas microbicides could also offer protection against other STIs which, of itself, would also contribute indirectly to preventing HIV, as the presence of other STIs increase the likelihood of HIV transmission. A HIV vaccine may only effective against one strain of HIV, whereas microbicides are likely to be effective against all strains of HIV. In addition, no one knows for sure when, or even if, a HIV vaccine might become available whereas a microbicide could available by 2007. Even after a HIV vaccine is discovered, microbicides and vaccines will have different and complementary roles to play in the response to HIV and other STIs globally.

Why can't we just promote male and female condoms more widely to reduce the spread of HIV and other STIs?

Both male and female condoms are very effective at preventing HIV and other STIs if used correctly and consistently. However, consistent usage with both types of condom is not easy. With male condoms in many contexts men don't want to use them and women are not in a position to negotiate for their use. Likewise, the female condom has been found in many settings to be difficult to use and critically the cost puts it out of the reach of many women, especially in the developing world. This is why microbicides research is putting a strong emphasis on the acceptability of microbicides to women - from the way the product is formulated, to where she prefers to access them, to the price she can afford to pay- to minimise the barriers to consistent usage when microbicides reach the market.

So would women want to use microbicides?

Market research carried out in the industrialised and developing world has clearly demonstrated a strong interest among women in a product that reduces the risk of HIV and other STIs, with the strongest interest coming from women living in the developing world. However, even in the industrialised world the Pharmaco-Economics Working Group of the Microbicide Initiative has calculated that between 20 and 30 per cent of women in the UK and Italy were interested in using a first generation microbicide when priced at five times the price of the male condom.

Who would benefit from using microbicides?

Women and their sexual partners. Women, wherever they live, would have a female controlled option to protect themselves and would not have to rely solely on the compliance of their male partners to reduce their risk of HIV and other STIs. With unprotected sex by far the most common route of HIV transmission worldwide, a microbicide offering even partial protection could have a profound effect on the spread of HIV: reducing the risk for HIV-negative women; reducing the potential of mother-to-child transmission; and reducing the risk of other STIs among HIV-positive women.

What is the likely impact of a first generation microbicide?

Researchers have developed a mathematical model that shows that if even a small proportion of women in lower income countries used a 60 per cent effective microbicide in half the sexual encounters where condoms are not used, 2.5 million HIV infections could be averted over three years. This translates into a cost saving of US\$2.7 billion in health care costs and US\$1 billion in productivity benefits over three years.

What would be the potential of microbicides in the EU context?

HIV/AIDS surveillance in the EU over the past decade documents a strong trend of increased heterosexual transmission of HIV, largely among recent immigrants, with women accounting for almost 50 per cent of all new HIV infections reported in 2001. Coupled with this we have, at best static, or rising rates of other STIs in the population. Microbicides would widen prevention options and give women, including young women, immigrant background women, and HIV-positive women, the possibility to act to reduce their exposure to HIV and other STIs.

How would microbicides be promoted and distributed?

The optimal scenario is that a first generation microbicide would be available over the counter in developing countries and by prescription in the industrialised world. Microbicides could be promoted and distributed by existing infrastructure in HIV/AIDS, reproductive and women's health.

How much will microbicides cost, and will people be able to afford them?

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 have rarely become widely available in developing countries until more than a decade after their approval in the US and Europe, an unacceptable delay for this life-saving technology developed primarily with public funds. Advocates are working with researchers and policy makers to emphasise 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.

What are the estimated costs for developing microbicides?

The Pharmaco-Economics Working Group funded by the Rockefeller Foundation has estimated that to ensure a high likelihood of generating a successful product by 2007, US\$ 775 million would need to be invested in direct product-related costs over the next five years. This calculation is based on evaluating the existing pipeline of products and does not include the discovery and exploitation of additional leads, work around access and product introduction, or the advocacy effort.

What are some of the outstanding priorities to get microbicides to market?

We need to accelerate the development of the products already in the pipeline to large-scale human trials so that we can prove the effectiveness of microbicides in reducing the risk of HIV and other STIs. Public and donor funding needs to expand to propel the innovation required, to fill the gap in investment that industry is unwilling to undertake at this stage. Access needs to be built into all stages of the development process of microbicides to ensure that when microbicides are introduced they will be accessible to the women that need them most at a cost that they can afford. A coordinated and sustained advocacy effort is needed to convince public and donor agencies to invest scarce resources, to maintain the interest of the scientific community, and to facilitate change to ensure that the policy environment is supportive to the speedy development of microbicides.

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**“There is a tide in the affairs of
men**

**Taken at the flood leads on to fortune
omitted, all of the voyage of their
lives are bound in shallows and in
misery**

**On such a sea are we now afloat
We must take the current while it lasts
Or lose the voyage of our lives”**

- William Shakespeare

**Recited by his excellency
Mr Lamuel A Stanislaus of Granada
at the United Nations Special
Assembly on HIV/AIDS June 2001**

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