



Microbicides: Meeting the challenge of HIV prevention in women

A briefing for Brussels-based institutions and organisations
Renaissance Hotel Brussels
7th October, 2005

REPORT OF THE MEETING

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I. Summary

This briefing on microbicides, organised by the Global Campaign for Microbicides and the International Partnership for Microbicides, took place at the Renaissance Hotel, Brussels on 7th October 2005. The event brought together 70 representatives of African governments, the European Commission, the European Parliament, Permanent Representations of the member states to the EU, Belgian Ministerial staff, pharmaceutical companies, research institutions and civil society to learn about microbicides and the vital role they could play in a comprehensive response to HIV/AIDS.

What are microbicides?

Microbicides is the term used to cover a range of products being developed to prevent the transmission of HIV and other STIs when used before or during sexual intercourse. A microbicide is a product, such as a gel or a cream, which could be applied topically to the vagina or rectum to prevent or significantly reduce the transmission of HIV and other disease-causing organisms during sexual intercourse. Microbicides could also take other forms, including films, suppositories, and slow-releasing sponges or vaginal rings. It is hoped that some microbicides will also allow conception so that women who wish to become pregnant can do so and protect themselves from infection at the same time. Safe and effective microbicides will help women substantially reduce their vulnerability to HIV infection during sexual intercourse. They do not exist yet, but are currently under development.

A summary of the meeting and copies of all the presentations can be viewed on the Global Campaign for Microbicides website: <http://www.global-campaign.org/microbicides-briefing.htm>

II. Presentations and Speeches

Welcoming Remarks - H.E. Maria Manuela dos Santos Lucas, Ambassador of Mozambique to the EU

Opening the meeting, Ambassador Maria Manuela dos Santos Lucas called upon her African colleagues to become involved in the microbicides cause: "We are here today to remind you that we are losing women on a daily basis in ever greater numbers; that we have failed collectively to prevent women and their children from succumbing to infection and to eventual death...Gender-specific development and a female-focused response must form the basis of future efforts if we are to break the deadly link between women, HIV/AIDS and poverty."

For the past two decades, **HIV/AIDS has affected more women worldwide than any other life-threatening infectious disease.** According to UNAIDS, at least 39 million people are living with HIV or AIDS; 19 million of them are women. Unless prevention efforts are drastically expanded, this number is expected to double by 2010.

Nearly two-thirds (64 percent) of all people living with HIV/AIDS are in sub-Saharan Africa, which constitutes only one-tenth of the world's population. Of these, women account for more than half the adults (15-49) living with HIV/AIDS (57 percent). For young women, the figures are even worse: 75 percent of young people infected with HIV are women and girls. In parts of sub-Saharan Africa young women are more than three times as likely as young men to be infected.

The rapid 'feminisation' of the global AIDS pandemic calls for a re-orientation of poverty reduction strategies and an urgent re-thinking of the global AIDS response. Gender-specific development and a female-focused response must form the basis of future efforts if we are to break the deadly link between women, HIV/AIDS and poverty. Without this re-prioritisation, it is unlikely that the Millennium Development Goals (MDGs), particularly those related to HIV/AIDS, health and gender equality, will be met. Achieving the MDGs is essential if the world is to have any hope of eradicating poverty and fostering development in resource-poor countries.

Ambassador dos Santos Lucas concluded by urging leaders and policymakers to see microbicides as a development tool. There has never before been a more urgent need to give women the power of prevention. But, the Ambassador concluded, "The time that it will take to get a microbicide depends on us. It depends on political will. On our political will."

Panel One: Microbicides - A critical component of HIV prevention

Why the ABCs are Failing the African Woman - Ms Françoise Welter, Policy Coordinator of the Global Network of People Living with HIV/AIDS (GNP+)

Françoise Welter was born in Rwanda and has been living with HIV for the past 12 years. She attributes her healthy life to the fact that she was diagnosed in Germany and not in Africa. With 20 years of experience in the United Nations and at the Global Fund, Ms Welter recently joined GNP+, an organisation dedicated to improving the quality of life for those living with HIV.

Rwanda is one of the countries most severely affected by HIV/AIDS, with women bearing the brunt of the epidemic. **Life expectancy is expected to drop to 32 within five years and by that time child mortality will have increased by 10 percent.** In Rwanda, as in much of sub-Saharan Africa, Ms Welter explained, gender inequality fuels HIV infection and makes women and girls powerless to protect themselves in the face of men whose physical and social power outweighs their own.

In such a setting, the mantra "Abstain, Be faithful and use Condoms" becomes irrelevant: "It is impossible for a woman who is being raped to 'abstain'. It is redundant to ask the married woman who was infected in the marital bed to 'be faithful' to her partner. And it is criminal to exhort the 'use of condoms' to women who are daily coerced into unprotected sex by partners who do not have to justify themselves."

Until a fully woman-initiated prevention method is available, Ms Welter argued, many women will be unable to take control of prevention. She described microbicides as a 'heaven sent' opportunity, but only if they challenge gender inequality and are available to every woman who needs them, including HIV positive women. "We, the stakeholders, must make sure that every woman living on the streets of Kampala, every sex worker in Nairobi, every female trader in Lilongwe, every illiterate woman in Kigali, every domestic in Johannesburg, has free access to microbicides."

To view Ms Welter's presentation in full, please consult:
<http://www.global-campaign.org/microbicides-briefing.htm>

The State of Research and Development of Microbicides for the Prevention of HIV - *Dr Zeda Rosenberg, CEO of the International Partnership for Microbicides (IPM)*

IPM was created in 2002 to accelerate the development of and access to safe and effective microbicides for use by women in developing countries. IPM is a 'Product Development Partnership' (PDP) that identifies best practice from, and collaborates with, both public and private sector partners in order to achieve its mission. IPM works across the development and access spectrum from initial research and development (R&D), to developing clinical trial sites and carrying out clinical trials, to facilitating regulatory pathways for licensure as well as ensuring that relevant public policies will be put in place to facilitate access to microbicides for women in developing countries, once they become available.

Most HIV infections are spread by unprotected sex and current prevention methods are male initiated and contraceptive. Women have no means to protect themselves if their partners do not use male condoms or allow female condoms to be used. Abstinence and being faithful are not likely to protect married women or those who are sexually abused. Women need a prevention tool that they can initiate themselves, like a microbicide. They also need a tool that comes in both contraceptive and non-contraceptive forms, to relieve those who wish to become pregnant of the untenable dilemma of choosing between protection from disease and the desire for children.

Microbicides are substances that can substantially prevent or reduce transmission of HIV when applied to the vagina. They could potentially be made in many forms: a gel or cream; a sponge; a film; a suppository; a ring or a diaphragm. They would be an important part of the comprehensive response to HIV/AIDS, as a female-initiated prevention method that could be applied before sex.

There are different ways in which microbicides could work and there are different categories of products, depending on their mechanism of action. Optimally they would prevent HIV from entering the cells lining the vaginal wall in the first place, although realistically a combination approach will be needed – similar to the 'cocktail' of drugs that proved most effective for treatment. Such a combination approach might well combine entry inhibitor compounds with others that limit the virus' ability to replicate once in a host cell (see further details see Dr Rosenberg's presentation in the appendix).

Dr Rosenberg explained that, for IPM, the choice of what compounds to pursue in the drug development process is very much driven by the need to develop a microbicide which will be safe and effective but also affordable, appropriate and therefore used by women. This means that factors such as the cost of manufacturing the compound, the aesthetics of a product (colour, smell etc) will also influence the design and choice of the product.

The drug development process is lengthy and very expensive with several different stages involved: 'pre-clinical' (in laboratory tests and in animals); before 'clinical' - moving into safety and large-scale efficacy trials in humans. Only after extensive pre-clinical work in the labs, resulting in a fairly high level of confidence that a compound looks active against HIV whilst not toxic, are compounds moved into clinical trials in humans.

Clinical trials are conducted in three phases. Phase I (often called initial safety trials) checks that the product does not cause any adverse reactions in very small numbers of healthy, low-risk

women (10-20). These trials are conducted in the country of origin of the product, usually Europe or North America. Phase II (usually referred to as expanded safety trials) takes approved products forward to be tested for adverse reactions in a larger number of women and over a longer period of time. Only if a product passes these safety tests can it move into Phase III trials where the ability of the product to prevent infection is examined for the first time (these are called effectiveness studies). These are large-scale trials involving thousands of HIV-negative women in areas where there is a high-risk of sexually transmitted HIV infection – such as sub-Saharan Africa. Enrolment in all trials is voluntary and all volunteers are given extensive counselling in HIV prevention, provided with free male and female condoms and have medical check-ups, which include treatment for sexually transmitted infections (STIs).

Unfortunately, the reality is that, even with counselling and access to current prevention methods, women are not always able to negotiate condom use and so will still be at risk of infection. The trials will compare two groups of women; those that receive the standard prevention package plus the experimental microbicide and those that receive the standard prevention plus a placebo (does not contain the experimental microbicide compound, but otherwise looks like the same product) – to assess the effectiveness of the microbicide. There are currently five candidate microbicides in Phase III trials and many more in earlier stages of drug development.

IPM is funded by governments and foundations and works with a wide range of international partners, including many R&D and advocacy partners in Europe (for a more extensive list of IPM donors and collaborators, see Dr Rosenberg's presentation in the appendix).

Annual investment in microbicide development needs to double from \$140 million to \$280 million per year. Dr Rosenberg concluded that with political leadership, sufficient financial resources, collaborative efforts and product development expertise, women in developing countries should have access to effective microbicides within the next five to ten years.

To view Dr Rosenberg's presentation in full, please consult: <http://www.global-campaign.org/microbicides-briefing.htm>

Responding to Policymakers' Concerns - Lori Heise, Director of the Global Campaign for Microbicides

The Global Campaign for Microbicides is an international coalition of NGOs and advocates working towards three goals: increased political will and funding for microbicides; a supportive policy environment for their development, introduction and use; and protection of the public interest and human rights as the science proceeds. As the civil society arm of the microbicides movement, the Campaign emphasises capacity building, community involvement in clinical trials, ethical issues and human rights. The Global Campaign and the IPM are co-conveners of the UNAIDS Global Coalition on Women and AIDS.

In her presentation, Ms Heise addressed four broad questions which are often raised by politicians, development specialists and policymakers when considering the usefulness of microbicides.

1. *Should we be concerned about introducing a method that is less efficacious (i.e. prevents fewer transmissions when used consistently and correctly) than condoms?*

Microbicides are sometimes described as an alternative to condoms that would be easier to use. However, the first generation of microbicides are likely to be only partially protective against HIV and STIs. Some public health officials fear that introducing a method which is more *attractive*, but less *protective* than a condom may cause people to abandon condoms in preference for microbicides, in what is termed 'condom migration'. However, research by the London School of Hygiene and Tropical Medicine suggests that **protection levels should increase, not decrease, with the introduction of microbicides.**

Protection is not just about the effectiveness of the method at the time it is used but also how often and how consistently it is applied. A method that confers a high level of protection but which is only used rarely, is less effective than a method that is less protective but used every time. The London School research shows that under most circumstances, substantial migration can be tolerated without increasing risk of infection. Condom migration could potentially be a problem only where condom use is high (above 70 percent) and microbicide consistency of use is low (less than 50 percent).

Currently, a substantial number of people are not using anything at all to protect themselves because condoms are unavailable or considered unacceptable by one or both partners. If all of these people begin to use microbicides, this should balance out the possible reduction in condom use by those few who switch methods. The experience from family planning is that with each new method, the number of unwanted pregnancies decreases. This is because there is greater choice and people are able to select something to suit their needs.

It is nonetheless important that microbicides should not be positioned as an alternative to the condom. The Campaign advocates the application of a harm reduction approach where microbicides are promoted as an 'adjunct' or back-up to condoms: "Use a male or female condom every time you have sex; if you absolutely can't use a condom, use a microbicide" or "use a microbicide with your condom for added pleasure and protection".

2. What public health benefits could reasonably be expected from the introduction of microbicides?

Research by the London School of Hygiene and Tropical Medicine has shown that **a 60 percent effective microbicide introduced into 73 low-income countries could avert 2.5 million infections over three years in women, men and infants.** This is the same as the number of women newly infected with HIV in 2004. Adult AIDS deaths in 2004 were 2.6 million.

This estimate conservatively assumes that microbicides are only effective against HIV (yet many will also protect against STIs, a known co-factor of HIV transmission), taken up by only one in five of those in contact with services (visiting clinics, in school, in prevention programs) and that those who use the microbicides only use them 50 percent of the time they have sex without a condom.

3. Who would most likely be the beneficiaries of microbicides?

There is much speculation about who would use and benefit from microbicides most – single women? Sex workers? Married women? HIV-positive women? Adolescents? Men?

The cruel fact is that the majority of the world's women contract HIV or STIs from a steady partner, rather than a casual or paying partner. Consistent condom use is universally difficult to achieve in emotionally close relationships – it seldom reaches more than 30-40 percent among couples who have taken part in condom promotion programs. In the case of HIV, repeated exposure to a single infected individual may pose more risk than having several

sex partners. Married girls have been shown to have more frequent sex, be less likely to use condoms and more likely to have HIV positive partners.

We are confident that people will use microbicides because of research that has been undertaken into this question, including a study funded by the European Commission. Women in countries all over the world have said that they would use them because they would be self-initiated, easier to negotiate and be more intimate. Most women would prefer not to keep their microbicide use secret from their partner, which is encouraging for those who think microbicides should improve existing gender relations.

4. What role can technology play in an overall HIV prevention agenda for women?

The field of microbicides is where issues of gender, technology and sexuality intersect. Microbicides often open up a discussion about sex and power. Echoing the statements of both Ms Welter and Ambassador dos Santos Lucas, Ms Heise concluded: "Microbicides can *begin* the discussion about sex and power. But, it can't end there. Changing the power balance between men and women is essential for real and sustained change."

To view Ms Heise's presentation in full, please consult: <http://www.global-campaign.org/microbicides-briefing.htm>

Panel Two: Microbicides and the European agenda: public and private responses

Chair: Mr. Michel Lastschenko, Special AIDS Envoy, Belgian Development Cooperation

Mr. Lastschenko introduced the second panel. In his introduction he described his mandate as Special AIDS Envoy, to better integrate Belgian international aid and foreign policies in the fight against HIV/AIDS. In doing so he stressed the need to bring together different actors from government, NGOs, the private sector and civil society as a whole, particularly including organisations representing people living with HIV/AIDS.

He emphasised that the crisis calls for an "integrated approach of education, prevention and treatment", stressing that **"most importantly we need to break the deadly cycle of infection and in particular curtail its spread among young people"**.

"We must do more" - increase public funds for research, encourage pharmaceutical companies and private laboratories to work with public universities and research institutions, and obtain "the massive private investment in research" – which is a necessity in the fight against HIV/AIDS. Belgium has long been involved in the efforts to develop microbicides. Researchers from the Institute of Tropical Medicine in Antwerp, the Universities of Ghent and Brussels, and Tibotec have been involved in many international research efforts for microbicide development.

Mr Lastschenko concluded his remarks by announcing Belgium's support of the next international conference on microbicides – Microbicides 2006 – that will take place in Cape Town, South Africa, in April 2006. He then introduced the speakers and invited the distinguished panel to share some thoughts based on their involvement in the microbicide research effort.

HIV/AIDS Research in the EU's 6th Research Framework Programme – *Dr Manuel Romarís, Directorate-General for Research of the European Commission*

Dr Romarís explained that **developing microbicides for HIV, like vaccines, is now a vital part of the EC's Programme for Action to Combat HIV/AIDS, TB and Malaria**. Under the current '6th Research Framework Programme' (FP6) there has been a four-fold increase in the earmarked funds for poverty-related diseases. A specific unit was created to work on poverty-related diseases and Phase II and III trials can now be funded through the European and Developing Countries Clinical Trials Partnership (the EDCTP).

In terms of microbicide development, FP6 already supports two networks of European scientists working on microbicides: EMPRO – the 'European Microbicides Project' – and the SHIVA project – 'Selection and Development of Microbicides for Mucosal Use to Prevent Sexual HIV Transmission/Acquisition'.

Dr Romarís highlighted the fourth and final call for proposals under FP6 which includes the call for an HIV/AIDS Vaccines/Microbicides Network of Excellence (deadline 9 November). This aims to increase the coherence of European actions and the cooperation with international efforts. He furthermore highlighted the EDCTP 2005 call for proposals – focus should be on Phase II/III trials in Africa and/or training and capacity building, within the context of HIV/AIDS, malaria and TB. There is currently an EDCTP grant for capacity building for Phase I/II trials of vaginal microbicides, funding up to 2.5 million euros per project.

Dr Romarís concluded by saying that in the next Research Framework Programme, FP7, which will run from 2007 to 2013 we should expect to see an increase in the budget, and an increased focus on prevention and treatment, as well as on highly innovative research. He also emphasised the important need for the EU to collaborate more with international efforts, such as IPM.

To view Dr Romarís' presentation in full, please consult: <http://www.global-campaign.org/microbicides-briefing.htm>

Partnering with IPM to develop a microbicide – *Dr Jens van Roey, Tibotec*

Dr Jens Van Roey, a medical doctor specialising in Tropical Medicine, has been involved in the response to the HIV pandemic since his days as a general practitioner in the town of Kikwit, Democratic Republic of Congo. He has served as programme officer for Africa to UNAIDS, and joined Tibotec Pharmaceutical Ltd. in order to advocate for the medical needs of the developing world. At Tibotec, he leads the Dapivirine (TMC120) microbicide programme and clinical research activities in Africa.

Tibotec is a pharmaceutical research and development company dedicated to the discovery and development of innovative new drugs for HIV/AIDS and other infectious diseases of high unmet medical need. Tibotec is based in Belgium and since 2002 has been a subsidiary of Johnson & Johnson. Tibotec is at the forefront of HIV research, with three novel antiretroviral compounds in advanced clinical testing. **In March 2004 Tibotec provided a non-exclusive licence to IPM to develop one of these compounds, Dapivirine, as a vaginal microbicide.** [A non-exclusive licence means that, even though IPM has development rights, other organisations can obtain, from Tibotec, similar rights to develop the Dapivirine as a microbicide.]

Dr Van Roey explained that Tibotec would not have been able to pursue the development of Dapivirine alone and that IPM was a very good partner to work with due to its clear mandate, sharp focus and flexibility. As a result, IPM has a fully paid up royalty-free licence to develop Dapivirine as a microbicide for sale anywhere in the developing world. [A fully paid up royalty-free licence means that IPM does not have to pay royalties or in any other way compensate Tibotec for sales of Dapivirine.] Tibotec retains the rights to sell the microbicide in the developed world. Tibotec and IPM are actively working together on carrying out clinical trials of Dapivirine in Africa (initial safety studies were first carried out in Belgium).

The Perspective of DG Development – Dr Lieve Fransen, Directorate-General for Development of the European Commission

Dr Lieve Fransen, Head of the Human and Social Development Unit within DG Development, began by stressing that HIV interventions have been unsuccessful for women for more than a decade: "In 1993 we issued the first call for proposals for actions on HIV addressing women in Africa. I knew at that time already that HIV interventions were failing women."

"Young women are the face of HIV," she said. "Being a woman, being young, being married, being poor and being African are the risk factors".

HIV magnifies inequalities. The B and C (Be faithful and use a Condom) prevention strategies have not been adequate to protect women, and adding A for Abstinence is even more ineffective. **Prevention for women has not improved since the 1990s.** This WAD, the focus is on prevention and the linkages between SRHR and HIV in fighting the epidemic will be highlighted. Dr Fransen further pointed out that the Global Fund "is there not just to provide treatments, but all HIV interventions. If countries demand microbicides, access will be possible."

In 1995 DG Development launched a study into microbicides and whether women would use them. It was important to know how to harness support from the private sector and to show the potential market that exists. The study showed a high demand for microbicides, even in countries like France and Poland.

The EU's recent policies to tackle HIV/AIDS have included poverty reduction, gender inequality, and an increase in ODA. Louis Michel, the Commissioner for Development has launched a new Programme for Action with an extra 20 billion euros to spend on AIDS, TB & malaria. This will focus on regulatory issues, and increase harmonization. It will seek to forge closer partnerships and launch a major new initiative on the gap in human resources. The new thematic programmes will also ensure that work on social and human development, including gender, health, education will continue. DG Development has already given five million euros to IPM. But new finances are needed.

What will it take to get microbicides to the people who need them? Answering her own question, Dr Fransen spelled it out:

- Money, both public and private
- Science
- Political leadership
- Partnerships
- Coalitions
- And above all, a strong women's movement!

Concluding Remarks - Anne Van Lancker, Member of the European Parliament, Chair of the Working Group on Reproductive Health, HIV/AIDS and Development

Summarising the key points of the briefing and leading on from Dr Fransen's presentation, Ms Van Lancker reiterated: "HIV has a woman's face. The reasons for this are connected to poverty, violence and the lower social and economic status of women. **Microbicides must be part of the response to HIV/AIDS**".

- Several International Conventions, Agreements and Declarations recognise the right to the highest attainable standard of health, including sexual and reproductive health. The right to protect oneself from HIV undeniably is part of these rights.
- By advancing women's rights, societies as a whole will benefit. New ways to protect women have the potential to slow down the devastating effect of HIV on families, communities and societies. This is essential to achieving the MDGs.
- The European Parliament has made some strong statements at the occasion of World AIDS Day and about neglected diseases. But Parliament's defence of microbicides as part of a comprehensive answer in the fight against HIV/AIDS needs to be more consistent.
- If we want to put microbicides into the hands of all who need them as quickly as possible, we will have to step up political and financial commitments, especially in the EU.
- Research, development and advocacy for microbicides are all severely under-funded. IPM, the Global Campaign and the Alliance for Microbicide Development estimate that annual funding for microbicide research and development must increase to \$280 million dollars in the coming five years, so that current levels must double to accelerate the pipeline, prepare clinical trials, manufacture pilot and bulk products and get communities in the host countries prepared to deliver these products.

"This is a human rights issue," said Ms Van Lancker. "It is about the right to the highest standard of health and the right to protect oneself against HIV".

Ms Van Lancker urged the participants to step up advocacy and to be more outspoken following the briefing event: "We have to look for new allies and build our partnerships". She urged the audience to work with the organisers of the event: "The Global Campaign and IPM certainly deserve our strong support".

Appendix A: Agenda

Appendix B: Attendance List

Appendix C: Biographies of the Speakers

Appendix D: PowerPoint presentations

Appendix E: IPM and the Global Campaign for Microbicides: Working in Europe to Make Microbicides a Reality