

What is MDP?

The Microbicides Development Programme (MDP) is a partnership of African and European researchers working together to fight HIV. MDP conducts clinical trials to test the safety and effectiveness of products which could help women protect themselves against this disease. We are currently carrying out a trial involving over 9000 women at six sites in Africa to determine the efficacy of a particular microbicide called PRO 2000.

MDP also engages in basic science, models the potential impact of microbicides and explores factors surrounding their acceptability. The MDP partnership includes social anthropologists, health economists and other experts who can help ensure that the women most in need of microbicides will find these products acceptable, affordable and easy to use. Uniquely, social science and marketing considerations have been integrated into MDP from the start.

What is a microbicide?

A microbicide is an HIV-prevention method specifically for women. It might take the form of a vaginal gel, cream, treated ring or other device. Unlike using a condom, a woman could insert the microbicide to protect herself from disease without making demands on her partner.

PRO 2000, the gel-based microbicide in the current MDP trial, showed a good safety profile in early tests in the USA, Europe, South Africa and Uganda. It may prove effective against herpes, chlamydia and gonorrhoea as well as HIV. Its developer is Indevus, a specialist pharmaceutical company in Massachusetts, USA.

Some future microbicides may also be usable rectally in men.

What is at stake?

The development of a prevention method for women could save millions of lives. Over 33 million people are infected with HIV and women are especially susceptible. 7000 new women get infected every day. In sub-Saharan Africa, where MDP concentrates its research, women make up almost 60% of adults living with this disease. Many are highly vulnerable to HIV despite the fact that they are married and faithful to their partners. Currently, women do not have a method of protection that they can use without making demands on their partners. A microbicide would put women's safety much more in women's own hands.

Microbicides and condoms

No matter how successful microbicides are found to be, they will be less effective than condoms. The strongest protection will be gained by use of both methods together. Women in our trial are urged to use both and their condom use has in fact increased significantly. But women are often unable to persuade their partners to use condoms and some avoid condoms because they wish to get pregnant. Some potential microbicides may be

appropriate for women who want protection from HIV without contraception but scientists are still awaiting data to confirm this.

MDP's Pan-African and north-south partnership

MDP comprises 14 research institutions or sites in Europe, South Africa, Tanzania, Uganda, Zambia and Mozambique. Coordinated jointly by Imperial College, London, and the Clinical Trials Unit of the UK Medical Research Council, the European partners also include the London School of Hygiene and Tropical Medicine, St. George's Hospital, London, and the Universities of York, Southampton and Barcelona.

African partners include:

- University Teaching Hospital, Lusaka, Zambia. Trial participants are employees of the Zambia Sugar Plantation as well as women from the local town of Mazabuka.
- Medical Research Council Uganda Virus Research Institute, Entebbe. Trial volunteers are drawn from 25 rural villages and most are couples in which the male partner sometimes has HIV and sometimes does not.
- African Medical and Research Foundation and National Institute for Medical Research, Mwanza, Tanzania. Most participants are women working in food and recreational facilities in 10 administrative wards of Mwanza City.
- The Africa Centre for Health and Population Studies, KwaZulu Natal, South Africa. Recruits to the study come mainly from a rural population of 80,000 people in the Centre's demographic study area.
- South African Medical Research Council, Durban. MDP works at Medical Research Council clinics in three semi-urban districts, Tongaat, Verulam and Isipingo. The clinics offer primary health care, and trial participants have been drawn from women who come for family planning and post-natal care.
- Reproductive Health and HIV Research Unit (RHRU), Department of Obstetrics and Gynaecology, University of Witwatersrand, Johannesburg, South Africa. Here, MDP has two trial sites, one within the grounds of a tertiary referral hospital in Soweto and the other at Orange Farm, a township 30 km to the south. Trial volunteers come from a large urban population spread over 31 districts.
- In Mozambique, new MDP sites at the rural Manhiça Health Research Centre and at Mavalane Hospital in the urban capital of Maputo plan to work with women aged 18-25, the age group at highest risk.

Who funds our work?

The UK government funds MDP through its Department for International Development (DfID) and Medical Research Council.

DfID's support represents a bold and innovative bid to address a longstanding problem. Historically, new drugs have not been affordable in the poor countries where disease can be most severe and, too often, drugs needed mainly in poor countries have not been developed at all. Drug research is vastly expensive. Microbicides sold at affordable prices might not be profitable enough to let pharmaceutical companies recover their research and development costs and these publicly listed companies have obligations to their shareholders.

MDP is a not-for-profit partnership. Our contract with the developer requires that PRO 2000, if successful, must be licensed in poor countries for distribution at prices just above cost. Our costs are very low compared to those in the pharmaceutical industry as our infrastructure is relatively modest, the UK partners receive academic-scale salaries and these are underwritten by our host universities.

Who is included in the current MDP trial – and why do people enrol?

Because cultural factors can affect the way a product is used, MDP is testing PRO 2000 in a range of environments – from urban townships like Soweto to semi-urban and rural communities in various African countries, and a sugar plantation in Zambia. MDP generally focuses on women in stable relationships, although one of our sites studies women who may have several partners. Another site focuses on couples, especially those where one partner is HIV-positive and the other is not.

Women give various reasons for signing up. They may want to qualify for the regular health checks, free condoms, counselling and hospital referrals provided by the trial. Some want to know their HIV status or may value the chance of added protection. Many have lost family and friends to HIV/AIDS and say they want to help find a solution.

How will we know if microbicides work?

The women taking part in our trial live in countries where the rate of HIV infection is extremely high. This means that, typically, these women are at serious risk of becoming infected in the course of their everyday lives. We will know our microbicide is effective if the groups of women who use our gel end up with fewer infections than groups not using it.

Informed consent

Our study teams use information sheets, visual aids and open-ended questions to ensure that each woman understands the risks and benefits of the study before she agrees to participate. Each time a woman visits the clinic, staff re-check to be sure she still understands what is happening and agrees to it. She is entitled to withdraw her consent at any time.

Participants' welfare

The safety of our volunteers is paramount. We are proud that 90% of our volunteers report using condoms as often as, or more than, they did before joining the trial. Our trial participants receive regular health check-ups, treatment for ordinary infections or ailments and referrals for specialist care as needed. Some women seem to have gained confidence through their participation in the trial and we have found a higher proportion of supportive partners than anticipated. Yet many women still cannot get their partners to use a condom every time and we hope that PRO 2000 will provide extra protection for these women in particular.

Community involvement

Each trial site employs liaison staff to ensure that local concerns are understood and addressed, that community values and practises are respected, and that messages from the clinic are properly conveyed. Additionally, each site has the benefit of an advisory board or group, consisting of local community leaders and stakeholders.

Management and oversight

A trial management group, consisting of senior representatives of all the sites, holds monthly teleconferences to monitor enrolment, retention, rates of infection, rates of pregnancy and possible side effects experienced by participants. Senior scientists visit all sites regularly to oversee participants' safety, review treatment decisions and ensure that international clinical standards are being met. Each laboratory is assessed annually to ensure that it follows Good Clinical Laboratory Practise and that any difficulties are addressed. On-site training is offered and experts are available round-the-clock by email or phone. Finally, the data-management system has four levels of error detection. (Double-data entry picks up discrepancies. Automatic checks detect missing data. Data are also checked centrally every two weeks and then analysed statistically.)

Other MDP bodies, again representing all partners, oversee programme and financial performance. A high-level steering committee, consisting of senior MDP investigators, community members and independent scientists, is responsible for scientific decisions including trial modifications, continuation or curtailment.

Two groups of eminent scientists provide independent oversight:

- An International Scientific Advisory Group reviews MDP's scientific strategy at least once a year, seeking (in part) to ensure that MDP complements other major initiatives in the microbicides field. Chair of the Group is Professor Anna Glasier, Director of Sexual and Reproductive Health, University of Edinburgh.
- An Independent Data Monitoring Committee meets routinely to review efficacy and safety data emerging from the trial, and ensure that ethical considerations receive

priority. This committee is chaired by Professor Sir Alasdair Breckenridge, Chairman of the UK Medicines and Healthcare products Regulatory Agency.

Each country where we work also provides oversight through ethics and government regulatory committees. Plans and procedures are approved in advance by the ethics committees and any adverse developments are reported to them immediately.

What good will come of this?

Microbicides will be less effective than condoms but too many women are powerless to insist on use of condoms and we hope that PRO 2000 will provide some protection for these women especially. The development of a prevention method for women would save millions of lives, especially if the use of a microbicide by women could be promoted alongside use of condoms by men. Even a partially effective microbicide could make a massive difference.

Important discoveries can take a long time. It took almost half a century to discover the cause of polio and develop a vaccine. Sir Almroth Wright worked for over 40 years to discover a vaccine for typhoid fever after the bacterium had been identified. Even when a drug is found not to work, key lessons are learned which contribute to later successes.

We have high hopes for PRO 2000 but, whatever the clinical outcome, the current MDP trial will leave a positive legacy. New laboratories have been equipped and accredited. Site staff have received experience and training in conducting clinical trials to the highest international standards. Many are being supported to acquire degrees and diplomas which will also advance their careers. Thousands of women have received counselling that will help them practise safe sex and lead healthier lives. They have a new understanding of their rights with respect to health care and know how to make the most of the care they receive. The trial has helped many women to discuss sex and HIV prevention options openly with their partners, and a surprising number report that their relationships have improved as a result.

Participants' voices

This thing (HIV) kills people in numbers, and people are vanishing. *(MDP participant)*

People will tell you that you can get HIV by kissing an infected person. ... I was ignorant about HIV before I came to the study. *(MDP participant)*

I like this clinic because we learnt many things. For instance, I was not concerned about condom use, but since I joined the study I always use a condom and am responsible for my life. *(MDP participant: Unemployed woman, age 32, Johannesburg, South Africa)*

I tell him that this medicine needs to be used together with condoms, so since he wants, he also wears. *(MDP participant: housewife, age 35, Zambia)*

I heard that there was thorough medical check-up provided in the clinic. Mainly that is what made me to join the study. The other thing is that I wanted to be part of the women taking part in this research of testing the gel. *(MDP participant)*

The reason I chose to come here is that they check everything inside a person's body, general health, they don't wait for you to complain about something before they look at it. *(MDP focus group participant, Johannesburg, South Africa)*

It is good to be a part of this study. You can get treated even for diseases you didn't know you had and it is not just HIV ... here you will gain more knowledge about your health and you will know how you were helped. *(MDP participant: Job seeker, age 28, Johannesburg)*

The clinic staff is friendly you always feel at home and you are able to share your personal problems with them. *(MDP participant)*

Both a male and female will have something for protection (against HIV). ... At the end of the day ... both of you have something to protect yourselves. I think that will help a lot. *(MDP participant)*

I will remember the time I spent in the study ... If it was possible I would rejoin the study again. *(MDP participant, age 23, Soweto, South Africa)*

The microbicide field

HIV is being fought on many fronts. Other microbicides are at various stages of testing, as are vaccines. Unlike commercial companies, non-profit ventures are able to share information and it is vital that we do so. Directors of other microbicide initiatives serve on MDP committees, while senior MDP scientists do the same for other trials. In addition, several organisations exist specifically to act as advocates or information clearinghouses for the field as a whole. A forum called the Quick Working Group links senior scientists. Other key groups are the International Working Group on Microbicides, the Alliance for Microbicide Development, the Global Campaign for Microbicides and its Microbicides Media and Communication Initiative.