This Advocates Brief have been developed by the Global Campaign for Microbicides in close collaboration with the other endorsing organisations listed here. While it articulates the current concerns and positions of these organisations, it is also a work in progress. We plan to re-issue this Advocates Brief in 2007, with revisions that reflect our collective perspectives on these issues.

HIV Positive Women and Microbicides

Microbicides have the potential to benefit HIV positive women by enhancing their sexual lives and helping reduce their risk of infection with new or resistant strains of HIV and other sexually transmitted infections (STIs). The development of effective microbicides, which would be user-controlled, is important for women who cannot always negotiate condom use with their male sex partners or who do not wish to use condoms (for instance, those who want to conceive). Ensuring that promising microbicide candidates are safe, affordable, and responsive to the needs of HIV-positive women will require ongoing and targeted research. Here are some of the ways microbicides might enhance the lives of HIV-positive women.

Microbicides could benefit women living with HIV, their partners and families.

Microbicides could help protect against HIV and possibly other sexually transmitted and vaginal infections that pose serious problems, especially when one's immune system is weakened. A broad-acting microbicide that is active against multiple STIs could help prevent some of these infections in HIV-positive women, and might even promote healthy vaginal conditions to ward off yeast infections or bacterial vaginosis.

Some of the candidate microbicides now in development may also eventually prove to be bi-directional – that is, capable of protecting women's sexual partners by disabling HIV in both semen and vaginal secretions.[1] Such a product could give HIV-positive women a way to reduce their male partners' risk of infection even if he chooses not to use condoms. Microbicides are not expected to be as protective as condoms – but they will be far more protective than nothing when used by people who aren't using condoms

Some of the candidate microbicides under development will also be contraceptive, while others will not. Condoms prevent pregnancy, so the only way at present for an HIV positive woman to fully protect an HIV negative partner while also attempting to conceive is by using alternative insemination (depositing semen in the vagina with a device such as a syringe or a diaphragm, rather than during intercourse). There are other ways for a positive woman to reduce the risk while attempting to become pregnant – such as having unprotected sex only right after ovulation (thus reducing the

[1] First generation microbicide trials – those enrolling women now – are designed to evaluate whether microbicides reduce HIV transmission from HIV positive men to HIV negative women. Separate trials would be needed to establish whether a product that works in this direction would also work to protect the HIV negative male partners of women already living with HIV.

number of times her partner is exposed). Taking anti-retroviral drugs may also potentially lower transmission risk by reducing the viral load in her vaginal fluids (although by how much is still unclear). But alternative insemination remains the only method currently available for introducing sperm into the vagina without any risk of transmission to a male partner.

A non-contraceptive, bi-directional microbicide would give HIV positive women who want to have children another option for safer pregnancy. Contraceptive microbicides, on the other hand, would give women another way to avoid an *unwanted* pregnancy. Microbicide researchers are also investigating the possibility of developing compounds that could be added to breast milk to make it safe for infant feeding.

Candidate microbicides must be proven safe for HIV positive women

Women living with HIV may have different needs for, and responses to, various microbicide products. We must understand these factors *before* microbicides become widely available, both because positive women will be using them, and because some women may not know their HIV status before using a microbicide. To date, only two of the three microbicides in large-scale efficacy trials have been through any testing to evaluate their safety for use by positive people. These preliminary safety trials must be followed by trials that generate long-term use data among women living with HIV so that researchers can adequately assess the long-term safety of such products if used by HIV positive women.

It must also be recognised that some types of microbicides (those that incorporate anti-retroviral drugs for vaginal application) may turn out not to be appropriate for use by HIV-positive women. It is possible that use of an ARV-based microbicide by an HIV positive woman could cause the development of drug resistant strains of the virus in her body, which might compromise her future treatment options. If testing proves that drug resistance is a problem (which is still an open issue), this particular type of microbicide might only be appropriate for HIV negative women.

With the exception of ARV-based microbicides, it is imperative that all candidate microbicides – even those intended to protect HIV negative women – be tested for safety among positive women and men before being allowed to advance to large-scale effectiveness trials.

Microbicide trials must protect the confidentiality and health of all participants.

Trials must take clear and specific measures to protect women's confidentiality and to counteract any public perception that women excluded from clinical trials are presumably HIV positive. Since positive people are stigmatised in many places, such assumptions may be both inaccurate and harmful to women and their families.

All trials include eligibility criteria. The current microbicide effectiveness trials enrol HIV negative women (for reasons described below). But several factors other than HIV status may also result in trial exclusion, such as:

- other health problems a woman may have,
- a desire to become pregnant in the near future (since trial participants are asked to use condoms),
- inability or unwillingness to adhere to the trial regimen (which often includes coming in for frequent clinic visits) or
- the woman's own decision not to participate.

Researchers and trial promoters need to make it clear to the communities in which they are working that exclusion from the trial could occur for any of these reasons and that people should not assume that women who don't participate must be HIV positive.

Clinical trial sponsors/researchers must further ensure that women who seroconvert during a microbicide trial have access to comprehensive HIV care including anti-retroviral drugs (ARVs) when appropriate. Microbicide trials also have a special obligation to attend to the sexual and reproductive health needs of participants, including offering to provide safe, appropriate contraception for trial participants.

Each clinical trial site should explicitly define the health care services that it will provide to trial participants and negotiate with community stakeholders (including relevant community and/or civil society groups) to determine the package of prevention services that will be provided to participants. It must also specify how access to this care will be ensured and provided.

How can HIV-positive women participate in effectiveness trials for microbicides?

In addition to gathering data about how safe microbicides will be for use by women living with HIV, we also need to give high priority to the question of whether they will protect the partners of HIV positive women.

Three candidate microbicides are currently in the large-scale trials designed to answer the most basic question -- whether it is possible for a vaginal product to reduce the risk of HIV transmission. In these efficacy trials, HIV negative women are followed to see whether they become infected over the course of a trial. It is important to note that all trial participants receive the best known prevention package – which consists of intensive condom counseling, supplies of free, high quality condoms and regular screening, and treatment if needed for STIs. The women are encouraged to use condoms and are never deliberately exposed to HIV or asked to forego condom use during a trial. However, some women nonetheless become infected because they are unable, despite assistance and counseling, to insist on consistent condom use with their partners.

Since male to female transmission is much more likely to occur than female to male transmission, enrolling HIV negative women is the fastest way of determining "proof of concept" – i.e. showing whether the basic concept of a microbicide is feasible. These efficacy trials won't show exactly how good the potential microbicide is at preventing male to female transmission – only whether the women who use it experience fewer sero-conversions than those who are provided with condoms and the inactive product (placebo).

If one of these trials demonstrates that the test product does help prevent male to female transmission, then it will be time to look at the opposite question – whether it can also prevent transmission from women to men. But a clinical trial to test this concept will look very different from these first trials. Instead of enrolling HIV negative women, these "next question" trials will have to enrol sero-discordant couples in which the woman is HIV positive and the man is negative. Their goal will be to see whether men become infected over the course of the trial.

Researchers can't just enrol men to answer this question because it will be their female partners, the HIV positive women, who will be inserting the candidate products into their vaginas. These women will need to be well informed about all aspects of the trial before giving their consent to use the test product. It would be unfair to the women if researchers just gave test products to men and asked them to get their partners to use it. It is essential that the women, themselves, receive all the available information about the trial and the test product and give their informed consent before using it.

Since these two trial designs are very different from each other, it is not possible to answer both questions (whether the product protects both women and men) in the same trial. But this doesn't mean that finding out whether HIV-positive women can use microbicides to protect their partners isn't a high priority. It just means that the questions must be asked and answered in order. While

waiting for the initial proof of concept to be established, the field can and should prepare itself to answer the second question by investing more money in gathering vital background data on vaginal immunology, ecology, viral shedding, the mechanisms by which HIV transmission from women to men occurs, etc.

What is the advocacy message?

HIV-positive women are some of the most vocal advocates for microbicides, as well as for expanded research on all aspects of HIV positive women's reproductive health. Together, we can advocate forcefully for the development of user-controlled interventions, such as microbicides, that promote sexual and reproductive health and rights. Although we aim for the ideal of sexual relationships based on mutual respect and responsibility, we recognise that many women need methods that give them greater power to protect themselves and their male sexual partners.

Some areas in which our advocacy is urgently needed now include:

1. Making sure that all candidate microbicides are tested for safety among positive women and men before being allowed to advance to large-scale effectiveness trials.

2. Demanding that all microbicide trials are designed to fully protect participant confidentiality and privacy, that the sexual and reproductive health needs of all participants are met and that women who seroconvert during the trial have access to comprehensive HIV care including anti-retrovival drugs (ARVs) when necessary.

3. Insisting that the microbicide field invest and engage now in gathering essential information on vaginal immunology, ecology, viral shedding, the mechanisms by which HIV transmission from women to men occurs, etc.

4. Calling on the field to commit to trials to assess the potential for bi-directional protection of any non-ARV-based candidate microbicides after they show proof of concept.