



Addressing Questions and Common Misperceptions about Microbicide Clinical Trials

1. To what extent will individuals and communities involved in trials directly benefit from participating in microbicide research?

Participants in trials will receive free, high quality condoms, risk reduction counseling and on-going sexual and reproductive health care (including treatment for sexually transmitted infections or STIs) during the trial.

Communities may benefit from improved health services and having better access to HIV information. Institutions in the communities in which the trials are held often benefit because trials help build research infrastructure, provide training to medical staff and often improve medical care facilities by enhancing their capacity to conduct clinical care and laboratory testing.

By its very nature, however, research is designed to answer important scientific questions for the future, not to focus on immediate benefits to trial participants. Nonetheless, volunteers are reimbursed for their time and travel costs. The appropriate level of reimbursement is decided locally after consultation with the community and relevant ethics committees.

There is also increasing consensus that host communities should receive fair benefits from their contribution to research, including preferential access to any product shown to be safe and effective.

2. How can researchers determine if a product works if people are counseled to use condoms during the trial?

If all trial participants were able to use condoms consistently, it would indeed be impossible to evaluate microbicide effectiveness. The very reason we need microbicides is that even with state of the art prevention counseling and access to condoms, many women cannot get their partners to use condoms every time. In addition, women who want to get pregnant cannot use condoms consistently.

The London School of Hygiene and Tropical Medicine recently compared all the studies that had been done on the impact of condom promotion among steady partners. They found that, even after receiving intensive condom promotion services, far fewer than half of people used condoms consistently with their regular partners. The rates of condom use are even lower among women and men in the general population who have not been exposed to condom promotion. These data show that men are generally less willing to use condoms with their long-term partners than they are with casual partners or paid sex partners.

Condom use with regular partner post intervention



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Location	Population	Condom Use	Notes
5 US Cities	high risk ?	17%	Consistent use
Nicaragua	general pop	7%	Consistent use
Rwanda	married women	22%	Regular use
Cameroon	youth	24%	Last any partner
Zimbabwe	sex workers	26%	Consistent use
USA	std clients	39%	Consistent use
Ukraine	IDUs	24%	High consistency
Bangladesh	sex workers	23%	Always use last week
Indonesia	sex workers	34%	Of sex acts protected
Tanzania	truck stop ?	43%	100% use last 5 acts

In clinical trials, the counselors make every effort to help women understand that they should not count on the test product to protect them from infection (since its effectiveness is unknown) and that using condoms is the best way to protect themselves.

Some women nonetheless become infected during the trial because they are unable, despite assistance and counseling, to insist on consistent condom use with their partners. That risk is not a *result* of the trial but rather a reality of life for millions of women.

Thus, microbicide trials are designed to test whether providing access to an experimental microbicide *in addition* to standard prevention (condoms, condom counseling and STI prevention) decreases risk of infection.

3. Will the products being tested be available and affordable to the people in the settings where the trials are taking place?

Traditionally there has been a long time lapse between testing new vaccines and innovations and their availability in the developing world. The HIV prevention field, however, is committed to eliminating this lag as much as possible with new HIV vaccines and microbicides.

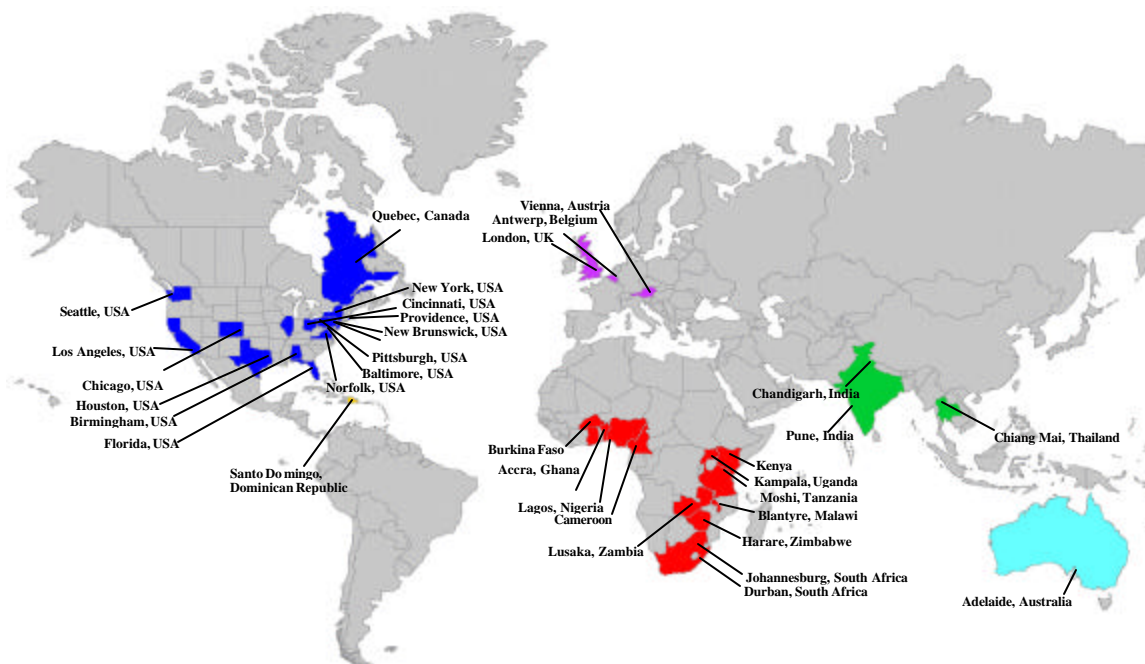
Public sector developers and advocates are working hard to ensure that innovative vaccines and microbicides will be available to the people who need them most, especially people in developing countries. This involves negotiating agreements early on with product sponsors that they will make the products available at cost or greatly reduced rates to governments and donors who wish to purchase them for their citizens. Because of public health need, microbicides may actually be made available in developing countries before the industrial world.

Most microbicide leads currently in testing are projected to be relatively inexpensive – similar to the cost of a condom. In most cases, the applicators and shipping cost more than the product itself. Efforts are underway to reduce these costs as well through innovative designs and local manufacturing. Key challenges will be financing, building demand among women and strengthening delivery capacity in countries to reach women (especially outside of urban areas).

MISPERCEPTION #1

Prevention trials are taking place in developing countries because it is cheaper to do so and poor people are easier to exploit.

Hundreds of communities around the world are participating in vaccine and microbicide trials. There is a concerted effort to distribute the burdens and benefits of research equitably. The map below indicates where clinical trials are taking place in 2006.



Source: Alliance for Microbicide Development

Large-scale effectiveness trials are not conducted unless smaller safety trials have already shown in both the industrial and developing world that the product appears safe for most women to use. It is common practice to do initial safety trials in the country of origin of the candidate microbicide, which is usually an industrialized country.

There are legitimate *scientific* reasons that most large-scale trials of microbicides are taking place in Africa – expediency is not the rationale. It is neither cheaper nor easier to conduct prevention trials in developing countries. Effectiveness trials have to be conducted where the risk of HIV transmission is high and where the primary route of infection is through heterosexual sex. Such communities exist largely in Africa and Asia.

In the United States and Europe, rates of infection among women are generally not high enough to conduct an effectiveness trial among women. Also, many women at high risk of HIV infection from

heterosexual sex in the United States and Europe also live in communities where intravenous (IV) drug use is common. This makes it problematic to enroll them in microbicide trials. If a woman who uses injecting drugs (even just occasionally) becomes infected during a trial, researchers would not be able to determine whether the infection occurred because of unclean needles or because the experimental microbicide product did not work. Concerns over exploitation of vulnerable populations in medical research are grounded in reality – there is a present and past history of trials being conducted in developing countries for questionable purposes. The HIV prevention field believes firmly that only research designed to potentially benefit citizens of the developing world should be conducted there.

MISPERCEPTION #2

Investigators must be actively exposing people to HIV in order to test microbicides.

Microbicide trials NEVER actively infect anyone with HIV. This would be completely unethical. Instead clinical trials are designed to evaluate whether giving people access to a microbicide in addition to condoms helps protect them from infection as they go about their daily lives. That is why trials must follow people for an extended period of time and take place in settings where HIV transmission is common. In fact, the chance of contracting HIV and other STIs substantially goes down for trial participants, regardless of whether they are receiving a placebo or an active drug. However, even with intensive prevention counseling and access to free condoms, women will still remain vulnerable to infection as they cannot always negotiate condom use or simply choose not to use them. This is the very reason that microbicides, and other alternative HIV prevention methods, must be developed.

MISPERCEPTION #3

Microbicide trials are unethical because they use a placebo.

All drug trials compare one group of participants who receive the experimental product to another group that does not. The goal is to determine whether the group that receives the new product fares better than the comparison group. There is no other scientifically valid way of testing drugs.

In some drug trials, this second group receives a placebo (a version of the product without the active ingredient) and in other trials the experimental product is compared to the standard drug or intervention used for that purpose. So for example, a new experimental painkiller might be compared to aspirin.

Ethically, placebos alone (with no additional intervention) may only be used as the comparator arm when there is no intervention known already to work. Recently some international trials have been criticized because they used placebos alone when other proven interventions existed.

Microbicide trials provide *all* participants with free condoms, risk reduction counseling and STI treatment. Therefore they compare standard prevention plus the experimental product to standard prevention plus a placebo. There is no group that does not receive state-of-the-art prevention.

The microbicide community has rejected as unethical a trial that would compare an experimental microbicide to a placebo without providing condoms or any other prevention services.



MISPERCEPTION #4

Participating in a microbicide trial increases one's risk of HIV infection.

Participants generally do not increase their risk of becoming HIV infected as a result of being in a microbicide trial. In fact, many reduce their risk as a result of receiving trial-provided condoms and condom counseling in their own language. However, some women will nonetheless become infected during the trial because they are unable, despite assistance and counseling, to insist on consistent condom use with their partners.

Women in both arms of a Phase III trial (those that receive the standard prevention package plus the experimental product as well as those that receive standard prevention plus a placebo) generally have fewer HIV infections than women in the general community because of the risk reduction efforts described above (e.g. free condoms, condom counseling and STI screening and treatment). Every effort is made to ensure that women understand that they should not count on the test product to protect them from infection (since its effectiveness is unknown) and that using condoms is the best way to protect themselves. If participants cannot insist on condom use with their partners, however, their HIV risk may continue despite their trial participation. That risk is not a *result* of the trial, but rather a reality of life for millions of women.

If, for whatever reason, a participant is directly harmed because of their participation in a trial—for example the experimental product makes them sick—sponsors are ethically responsible, under internationally agreed upon guidelines, for providing medical care and compensation for the harm.

MISPERCEPTION #5

All clinical trials are sponsored by large pharmaceutical companies that have lots of money.

While it is true that many large pharmaceutical companies conduct clinical trials in developing countries, microbicide trials and most HIV vaccine trials are sponsored by not-for-profit or academic institutions with public health goals. Although some for-profit companies are involved, they are generally small and have to partner with government and foundations to get their products tested.

Presently no large pharmaceutical companies have invested substantially in the development and testing of microbicides. All research and testing is conducted by academics, not-for-profit organisations or small biotechnology companies – all of which depend on government grants and charitable foundations to support their research. Thus, most microbicide research is motivated by public health goals and objectives, not private gain.