Fact Sheet #18

Addressing Common Questions and Myths about Microbicide Clinical Trials

Global Campaign FOR Microbicides

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

Participants in trials will receive free, high quality condoms, state-of the art condom counselling in their own language and on-going sexual and reproductive health care during the trial.

Communities may benefit from access to trial-provided health services and increased access to HIV information. Institutions in the communities hosting trials 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. Volunteers are compensated for their time and travel costs. The appropriate level of compensation 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 counselled 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 counselling and access to condoms, many women cannot get their partners to use condoms every time.

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 couples in long term partnerships were able to use condoms consistently with each other. 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.

In clinical trials, the counsellors 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 counselling, 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.

3. How safe are the products that go into Phase III effectiveness trials?

The Phase III effectiveness trial works by comparing two groups (1) those receiving the best known prevention package (counselling, condoms, and STI treatment) plus the candidate microbicide and (2) those receiving the best known prevention package plus the comparator gel. The comparator gel looks just like the drug being studied but does not contain the active ingredient.

Candidate products are not allowed to enter Phase III effectiveness trials until they go through a long and labour-intensive series of tests, including laboratory tests, multiple tests in animals, and a carefully staged series of clinical safety trials in human beings.

Despite this, it is still possible (although very rare) for product safety concerns to emerge during Phase III. Independent Data Monitoring Committees are in place to look for emerging evidence of problems as the trial progresses. If evidence appears, the trial is stopped immediately. Provisions for on-going care for any trial participants who seroconvert during a trial (for whatever reason) are put in place before a Phase III trial starts. Advocates have played a key role in getting these safeguards implemented and are continuing advocacy for still better participant protection.

For more information on how scientists evaluate safety, please see the GCM issue brief: Evaluating Microbicide Safety (Available for download at: www.global-campaign.org/Cellulose-Sulfate.htm).

4. If they are shown to work, 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.

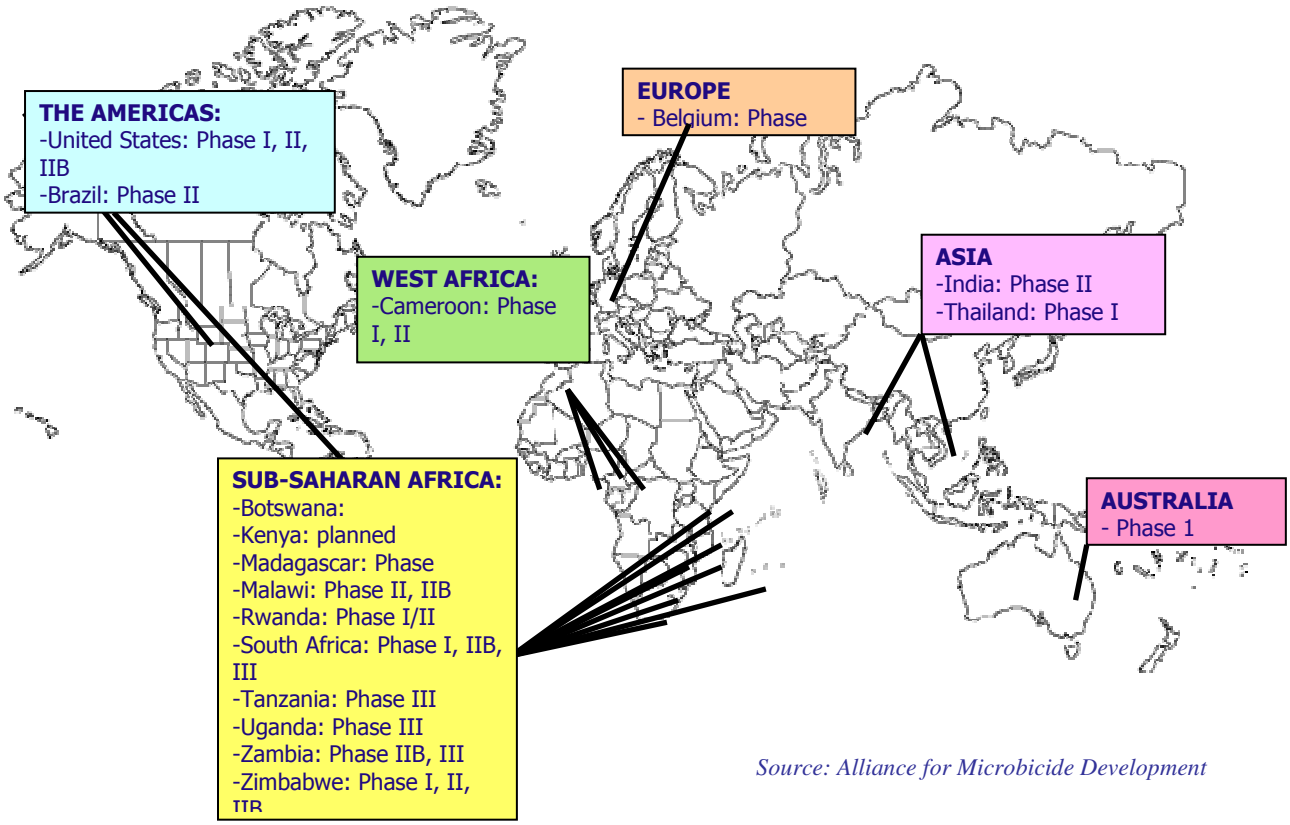
Public sector developers and advocates are working hard to ensure that innovative vaccines and microbicides will be available to the people who need them most. This involves negotiating agreements early on with product sponsors that they will make the products available at cost or greatly reduced rates to governments and donors who wish to purchase them for their citizens.

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.

MYTH #1

Microbicides 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 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 2008.



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 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 industrialised 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 Sub-Saharan Africa and in some communities in India and South East 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. If a woman who uses injecting drugs (even just occasionally) becomes HIV positive during a trial, researchers

would not know whether the infection occurred because of unclean needles or because the experimental microbicide product did not work. This makes it problematic to enrol IV drug users in microbicide trials.

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 microbicide field, however, believes firmly that only research designed to benefit citizens of the developing world should be conducted there.

MYTH #2

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

Microbicide trials NEVER actively infect or expose anyone to 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 heterosexual HIV transmission is common.

MYTH #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 criticised because they used placebos alone when other proven interventions existed.

Microbicide trials provide *all* participants with free condoms, risk reduction counselling 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 any trial that would compare an experimental microbicide to a placebo without providing condoms or any other prevention services.

MYTH #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 counselling in their own language. However, some women will nonetheless become infected during the trial because they are unable, despite assistance and counselling, 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 counselling 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 function of the very high background rate of HIV transmission in the participating communities.

In rare cases it is possible that a woman's risk may be increased in Phase III effectiveness trial if the product being tested causes safety concerns that were not evidence in the safety trials done prior to the Phase III trial.

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.

MYTH #5

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

While 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 yet invested substantial funds in microbicide research or testing. 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.

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What is the Global Campaign's role in clinical trials?

One of the Global Campaign for Microbicides' core goals is to ensure that as the science proceeds, the rights and interests of trial participants, users and communities are fully represented and respected. As microbicide trials roll out, the Global Campaign is committed to:

- Giving voice to community and civil society perspectives on trial design and ethics issues
- Forging consensus around ethical debates that could delay progress
- Negotiating the difficult line between urgency of the HIV epidemic and maintaining rigorous ethical standards
- Building capacity in activist/community sectors for ethical deliberation and debate

For more information:

For more information about the Global Campaign's work in this area, please go to our Ethics and Community page, *http://www.global-campaign.org/ethics_community.htm*.