

Managing Expectations Around Microbicides

Sustaining public support for prevention research while communicating the complexity of the research task will require a delicate balance of honesty and optimism.

- Chris Collins, Social Issues Over the Long Haul of Human Trials, 1996

The challenge for the microbicide field is to find the correct balance between building enthusiasm and political support for microbicides, while avoiding raising unrealistic expectations. Unfulfilled expectations can backfire and create doubt that could erode continued financial and community support.

A case in point is the field of HIV vaccines, which initially benefited from people's familiarity with the concept of a vaccine and their working assumption that like many childhood vaccines, an HIV vaccine could provide lifelong protection from infection.

The quest for an HIV vaccine, however, has been repeatedly stymied and scientists are now investigating products that might *delay* disease progression without fully *preventing* infection. While still providing tremendous public health benefit, such a vaccine is more difficult to explain to consumers and will likely fall short of general expectations.

Media and advocacy outreach around microbicides must similarly be attentive to the complex nature of drug development. Public discussion of microbicides must be sensitive to the desperation and powerlessness that many women feel in the face of their current HIV risk and their lack of ability to protect themselves. In this environment, it is irresponsible and potentially exploitative to be overly optimistic about the characteristics and likely availability of microbicides.

What then are realistic, but inspiring, messages we can use to describe the potential for microbicides? And what other information must we incorporate in our advocacy and media work to help the wider public understand the realities of drug development?

This fact sheet contains several key messages that you can use to express clear and realistic expectations about microbicide in advocacy and outreach regarding:

- Timing of microbicide availability
- Drug development generally
- Nature of clinical trials
- Likely microbicide effectiveness
- Cost of a microbicide
- Attributes of a microbicide

Regarding timing of microbicide availability:

1. Only a few microbicide candidates¹ are in the last stages of testing to determine whether they are effective (which can take up to 4 years). We do not know yet whether these candidates will work. If a trial shows that a microbicide does work, at least another two to four years will be required for individual countries to go through their own regulatory and manufacturing processes to make the microbicide available. Due to these individual country processes, it must be noted that a microbicide will not be available in all countries at the same time and not all people within a country will get it at the same time. It is likely to be made available to some women and not others during introduction and scale-up
2. The microbicide community is working hard to accelerate development and ensure that products get to those who need them as quickly as possible.

¹ For more information on the exact number of candidate products in the pipeline, please visit the Alliance for Microbicide Development's website at www.microbicide.org

Regarding drug development generally:

- Drug development is a long and complicated process. It can take 10 to 15 years between discovery of a promising lead and its availability on the market.
 - a. Many candidates fail before one ever proves both safe and effective
 - b. Candidates routinely drop out of contention because they emerge as unsuitable during some stage of testing. This is why the microbicide field needs many different candidates, which use different mechanisms of action, moving forward through development and testing at the same time. Drug developers call this a diverse product pipeline.
- It generally takes even longer for drug innovations to become available to people living in the developing world.
 - a. Historically, it has taken decades for the benefits of scientific innovation to trickle down to the developing world. Some innovations never reach those who need them.
The microbicides field is committed to expediting the widespread availability of any effective product, reaching those who are most in need first.
 - b. Public sector developers and advocates are working hard to ensure that innovative vaccines and microbicides will be accessible and affordable to the people who need them most. This involves negotiating agreements early on with product sponsors to ensure they will make the products available at cost or at greatly reduced rates to governments and donors who wish to purchase them for their citizens.
 - c. Given the urgency of the epidemic in sub-Saharan Africa, it is possible that a microbicide would be licensed first for use in a country such as South Africa, rather than in the United States or Europe.

Regarding the nature of clinical trials:

- The process of testing a new product for safety and effectiveness is similarly long and complex. It generally takes *many* clinical trials—some, if not most, involving leads that prove to have problems or don't work—before finding a drug that can address a new health area, or in the case of microbicides, a new way of preventing HIV transmission.
- Candidate microbicides pass through a series of rigorous tests in the laboratory and in animals before they are allowed to be tested in human beings.
- There are three Phases of human clinical trials:
 - a. Phase I trials determine whether the product is safe (does not cause immediate harm) if used by a small number of healthy low risk women over a few weeks.
 - b. Phase II trials also test for safety of the product, but over a longer time and with a larger number of women, some of whom may have higher risk factors.
 - c. Phase IIb trials, also called proof-of-concept trials. Larger than a Phase II study but often only half the size of a full-scale Phase III trial, a Phase IIb study enrolls enough people to offer a suggestion of whether the microbicide can prevent HIV infection.
 - d. Phase III trials enroll thousands of people in several sites. These trials measure effectiveness - that is, whether or not the microbicide actually works in the course of normal use to prevent HIV and/or STIs.
 - e. If the product appears to cause harm, research on that candidate is stopped and the product is dropped from consideration as a potential microbicide.
- Even when a clinical trial suggests that a drug is efficacious, there are many more steps that must be completed before it can be made available to consumers:
 - a. Frequently, clinical trials need to be repeated to confirm their results or to test the finding in different populations.

- b. The drug must be reviewed and licensed for use by at least one drug regulatory agency.
 - c. The product must be manufactured in large quantities, registered and introduced in different settings.
- Even if a trial does not yield convincing results of effectiveness, it nonetheless increases knowledge. Each trial builds the evidence base and strengthens the field's ability to plan and mount successful trials in the future.

Regarding likely microbicide effectiveness:

- The early microbicides products are likely to reduce risk of transmission by no more than 40 to 60 percent. But even a partially effective microbicide can provide substantial protection from HIV, especially if used consistently.
- Even a 60% HIV/STI efficacious microbicide could avert 2.5 million HIV infections over 3 years, if introduced into 73 low-income nations, according to modelling by the London School of Hygiene and Tropical Medicine.
- The goal is to improve incrementally both the effectiveness of microbicides and the range of sexually transmitted infections that they are effective against. Just as the first generation of hand-held calculators were expensive and bulky when first introduced, microbicides will likely become more effective, more user-friendly and cheaper over time.
Note: For health or HIV-aware audiences, one can draw the analogy to HIV drugs rather than hand held calculators: "Just as the first generation of anti-HIV therapies like AZT, were cumbersome and less than optimal..."
- The future of prevention is in combination products. Just like it takes several drugs used in combination to keep already HIV infected individuals healthy (drug cocktails), microbicides will likely be most effective when they combine two or more mechanisms of action (ways to inactivate the virus).

Regarding likely cost of a microbicide:

- Most microbicide leads currently in testing are projected to be relatively inexpensive – similar to the cost of a condom. Given its public health mission, the microbicide field only advances leads that will be affordable for consumers.
- In most cases, the applicators and shipping cost more than the product itself. Efforts are underway to reduce these costs even further through innovative designs and identifying capacity to manufacture products in developing countries.
- 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.

Regarding likely attributes of a microbicide:

- The first microbicide available will likely be in the form of a gel that is inserted in the vagina before sex using an applicator (like a tampon or today's yeast infection medications).
- Scientists are developing innovative means to deliver microbicides - for example through a sponge or vaginal ring that could be left in place for a month or more. Vaginal rings are already in human testing and daily-use gels that are applied independent of sex are already in extended safety trials.
- Many women say that they would not try to use a microbicide secretly - they would want their partner to know. Nonetheless, women articulate a great advantage to having a method they can use that does not require a man's active cooperation at each act of intercourse. The prospect of a

woman-initiated method means that the discussion on use can happen outside of the bedroom and women can take prevention into their own hands.