

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:

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| ?? Timing of microbicide availability | ?? Cost of a microbicide |
| ?? Drug development generally | ?? Attributes of a microbicide |
| ?? Nature of clinical trials | ?? Resource needs of the field |
| ?? Likely microbicide effectiveness | |

REGARDING TIMING OF MICROBICIDE AVAILABILITY

1. If one of the five candidates that are currently in advanced clinical trials proves to be effective, a microbicide could be ready for distribution in a handful of countries by the end of 2010.¹
2. If the current set of products does not prove effective, the time horizon will be longer (although there are several second-generation leads already in human testing).

¹ Results from the trials furthest along could become available in late 2007 or 2008, but it will take additional time for the products to be reviewed and approved for licensure.

3. The microbicide community is working hard to accelerate development and ensure that products get to those who need them as quickly as possible.

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 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.
- d. 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 first generation of microbicides is 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 modeling done 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.

REGARDING RESOURCE NEEDS FOR THE FIELD

- ✂✂ In 2000, roughly \$65 million total was being invested globally in microbicide research, development, testing, policy and advocacy. The vast majority of investment was then, and still is, provided by governments and the philanthropic sector.
- ✂✂ By 2004, global investment had more than doubled to \$142 million annually, due to sustained activism and growing scientific promise.
- ✂✂ Projections developed by the International Partnership for Microbicides (IPM), the Alliance for Microbicide Development and the Global Campaign for Microbicides estimate that the global annual investment to ensure timely development of a safe and effective microbicide must re-double to at least \$280 million per year over the next five years—and remain at approximately \$280 million a year until satisfactory microbicides are licensed.
- ✂✂ The \$280 estimate assumes that:
 - \$130 million a year is needed for research (discovery and pre-clinical development)
 - \$120 million a year is needed for clinical testing
 - \$20 million a year is needed for clinical trial site development (for 5 years only)
 - \$10 million a year is needed for advocacy and policy (this represents more than a tripling of the annual investment in this category)

NOTE: These figures do not include any funding for purchase or distribution of a microbicide once it is licensed. That will represent an additional cost.