

Rectal Microbicides: Investments & Advocacy

Executive Summary

This report was prepared on behalf of
the International Rectal Microbicide Working Group

April 2006



Technology should be the friend of all people, not solely a tool of the dominant group. We must demand that the full resources of our nations be committed to the development of new prevention technologies such as rectal microbicides that will allow us another way to care for each other and keep each other healthy.

—Eric Rofes, professor, author, and advocate for men's health

Women's need for protection against sexually transmitted pathogens, like the need for contraception, varies greatly from one individual to another, and can change over the course of a lifetime. The availability of both a rectal and vaginal microbicide will ensure that women have options, should they need them, for protection against HIV and other STDs. For this reason, an investment in research on rectal microbicides is essential.

—Geeta Rao Gupta, leading global authority on women's development

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Rectal microbicide research is a burgeoning pursuit with attendant opportunities and challenges. Recent scientific discoveries need to be matched with the societal and political will and funding to ensure rapid advancement of a potentially life-saving biomedical intervention.

Because sexual intercourse accounts for the vast majority of HIV transmissions worldwide, a rectal microbicide could benefit global health by preventing HIV infection in the two most vulnerable populations: heterosexual women and males who have sex with males (MSM). The at-risk population of women is potentially fivefold greater than that of MSM because of the sheer number of anal intercourse (AI) acts and the limited use of condoms. Even more significant is the associated risk of HIV transmission through anal intercourse, measured at 10- to 100-fold that of vaginal intercourse.

Increasing global HIV rates testify to the need for new prevention tools. Since the pandemic began, over 60 million people have been infected with HIV, more than 25 million people have died, and 5 million people were newly infected with HIV in 2005. Rectal microbicides are envisaged as one prevention tool to be used in combination with others to achieve maximum protection against HIV. This combination approach to prevention mirrors the combination strategy used in the treatment of HIV with antiretroviral therapy.

Opportunities

There are 16 vaginal microbicides in human trials, 5 are in efficacy trials—the final step before licensure—, and over two dozen are in the research pipeline, waiting to be evaluated in humans. It is possible that the discovery of a safe, effective vaginal microbicide is imminent, perhaps even as early as 2010.

Behavioral scientists agree that once a vaginal microbicide becomes available, some people are likely to use it rectally in the hope of achieving protection during anal sex. Because the rectum and vagina are two different biological environments, potentially this “off-label” use could cause harm to the rectum and help facilitate HIV infection. For this reason, products will need to be evaluated in both environments for safety and efficacy.

AI is practiced by up to 30% of heterosexuals in many cultures. Because women make up the majority of receptive anal partners they—in addition to MSM—are in need of a rectal HIV-prevention method. The same requirements for the discovery of a vaginal microbicide can be applied to the need for rectal protection: until a woman can negotiate condom use consistently with her male partner(s), she will need protection that she herself can control with or without his knowledge or active participation.

Rectal microbicide research is a relatively new field. The first human studies, using nonoxynol-9, were conducted in 1999. Despite its short history, the field is making rapid progress through its capacity to leverage significant amounts of basic science research from the vaginal microbicide development field. The relationship between the two pursuits is synergistic, with vaginal microbicides taking precedent, followed directly by development of rectal microbicides. For example, the first rectal microbicide candidate slated to be tested in human trials this year, UC-781, entered the microbicide research pipeline in the late 1990s and is currently undergoing vaginal safety testing.

Two landmark studies in animals show that topical cyanovirin and a combination of tenofovir/FTC given orally appear to prevent rectal HIV transmission in macaques. Both lend hope to the feasibility of proof of concept of rectal microbicides in humans.

The discovery and efficient distribution of a rectal microbicide could mean the reduction of HIV transmission throughout the world. Recent mathematical modeling suggests that a rectal microbicide with greater than 30% efficacy would significantly reduce the number of secondary HIV infections occurring in high-risk settings such as bathhouses. The prevention of HIV infections could not only save lives, but could save on costs by avoiding loss of workplace productivity and reducing health-care spending.

Researchers believe that midway through 2007, gaps in knowledge such as rectal-safety indices will have been discovered and candidates will be poised for fast track research. It is essential that donor countries and institutions support these efforts.

Challenges

The proof of concept that a microbicide—vaginal or rectal—will work in humans has yet to be achieved. Efficacy studies are time-consuming and expensive.

Large pharmaceutical companies and smaller start-ups that usually fund new drug development have shied away from microbicide research, as they have with vaccine research, because these interventions are perceived as too much financial or liability risk for too little profit. As a result, rectal microbicide funding is reliant on government and philanthropic grants.

Although the rectal microbicide field is in some aspects in its infancy—still establishing correlates of safety—funding needs to be forthcoming to ensure research and development scale-up.

There are several factors that can explain the relative delay in the development of rectal microbicides, including sociocultural taboos surrounding anal intercourse; the more complex scientific challenges posed by rectal microbicides compared with vaginal microbicides; and the historical lack of concerted advocacy efforts and clear articulation of demands for rectal microbicides from communities.

Challenges remain to mobilize advocates and educate the public and policy makers on the importance and potential of a rectal microbicide. In doing so, advocates must dispel the myth that only MSM engage in AI, while also battling the homophobia and denial that prevents key stakeholders from addressing the health needs of women, MSM and gay men who engage in anal sex.

Findings

In an unprecedented effort, this report quantifies current rectal microbicide expenditures compared with projected costs to develop a safe and effective product. Findings will be used as a reference from which to pose recommendations and measure progress.

- Findings show that total rectal microbicide research disbursements for 2006 are \$7.2 million. It is estimated that it will cost at minimum \$350 million over the next 10 to 15 years, or roughly \$35 million a year to develop a comprehensive rectal microbicide research program. Annual spending needs to increase fivefold to ensure timely discovery and development of a rectal microbicide.
- The academics, small biotech firms, and nonprofit organizations that are currently pursuing rectal microbicide research are doing so with limited funding from a handful of government and foundation donors. The U.S. public sector is the largest donor, contributing \$33.1 million between 2000 and 2006, or 97.4% of total rectal microbicide expenditures. The National Institutes of Health contributed \$30.8 million, and the Centers for Disease Control and Prevention gave \$2.3 million between 2000 and 2006.
- The American Foundation for AIDS Research (amfAR) was the only philanthropic contributor, awarding a total of \$739,649 between 2000 and 2006.
- The European Commission, other countries, and multilaterals, have not contributed directly to rectal microbicides through detectable, traceable lines or quantities.
- The commercial sector contributed \$100,000 in in-kind donations between 2000 and 2006.

Summary of Recommendations

The goal of developing a safe, effective rectal microbicide depends not only on advances in science, but also on societal, financial, and political support. Government officials, political leaders, and civil society must become engaged in order to create an encouraging environment for developing, approving, and distributing a rectal microbicide.

The International Rectal Microbicide Working Group recommends the following urgent actions in order to discover a rectal microbicide within the next 10 to 15 years.

Donors must:

- Provide a minimum of \$350 million for targeted rectal microbicide research funding over the next 10 to 15 years, or an average of at least \$35 million per year to build a comprehensive rectal microbicide research program.
- Provide transparency and an increase in institutional commitment to explicitly fund rectal microbicide development.
- Commit to supporting phase 1 rectal safety studies for all vaginal microbicide candidates being evaluated in phase 2B/3 efficacy trials.

International nongovernmental organizations must:

- Form a body to specifically track rectal microbicide development, to ensure funding, and to coordinate research, regulatory approval, and advocacy.

Researchers must:

- Recruit new scientists to the field and promote rectal microbicide research within the scientific community.
- Initiate ideas for grant proposals to create demand for funding.

Advocates must:

- Reach out to affected communities to educate and to promote rectal microbicide trial preparedness.
- Promote global, national, and regional surveillance efforts to determine percentage of HIV infections attributed to AI in order to better assess the need for rectal microbicide development.
- Raise awareness, educate, and mobilize communities to foment a stronger, more visible demand for rectal microbicides and to elevate the profile of microbicides among policy makers.
- Ensure linkages to the broader microbicide movement and to advocates working on other prevention technologies.

Regulatory agencies like the U.S. FDA, the EMEA, and others must:

- Create support and development guidelines to accelerate the study and licensure of rectal microbicides.
- Request that all New Drug Applications for vaginal microbicides include at least one rectal safety study as part of the submission package.

The U.S. Congress must:

- Pass the Microbicide Development Act, and other countries should consider similar legislation.

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