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special/perspective:

Robert M. Grant, Dean Hamer, Thomas Hope, Rowena Johnston, Joep Lange, Michael M. Lederman, Judy Lieberman, Christopher J Miller, John P. Moore, Donald E. Mosier, Douglas D. Richman, Robert T. Schooley, Marty S. Springer, Ronald S. Veazey, and Mark A. Wainberg
Whither or Wither Microbicides?

Science 2008; 321: 532-534 [\[Abstract\]](#) [\[Full text\]](#) [\[PDF\]](#)

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▼ **Challenges in HIV-Prevention Microbicide Research**

Polly Harrison, John W. Mellors, Barbra Richardson, Benoit R. Masse, Quarraisha A. Karim, Salim S. A. Karim et al. (17 December 2008)

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Biotech is a constantly evolving industry...

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Challenges in HIV-Prevention Microbicide Research

17 December 2008



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R. M. Grant *et al.* (Special Section on HIV/AIDS: Follow the Money, Perspectives, "Whither or wither microbicides?", 25 July 2008, p. 532) raise provocative points on how candidate microbicides are evaluated and selected for testing in effectiveness studies, and how microbicide research should be redirected for success. The authors make valid observations and provide a valuable platform for candid discussion of the challenges in microbicide research—challenges also germane to other HIV prevention research approaches, including pre-exposure prophylaxis.

Product selection: We agree that stringent criteria must be applied to the selection of microbicide products for testing in effectiveness trials. BufferGel, Carraguard, cellulose sulfate, PRO2000/5, and SAVVY were selected for evaluation early in this decade based on the best scientific tools and knowledge then available. Since then, testing algorithms and assays have become more sophisticated. This evolution and what we are learning from current trials are already guiding the identification and selection of newer candidates.

Animal models: The authors recommend preclinical studies in Non-Human Primate (NHP) models as essential to establishing the biological plausibility of

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candidate microbicides. As with use of NHP models to evaluate HIV vaccines, NHP models for microbicides are not yet validated, no consensus protocol exists, and the model is subject to substantial variability. While NHP studies are critical to generating and testing hypotheses, we see them as parallel, not primary, streams of evidence supporting selection of products for effectiveness testing.

Development of combination approaches: Strategies for HIV prevention must consider both risk and benefit, a balance that, simply put, differs considerably for HIV-infected vis-à-vis -uninfected individuals. Development of combination approaches to treatment has been critical to the improvement of HIV therapies. Uninfected individuals who will use drugs for prevention, whether applied topically or orally, must have assurance that chronic exposure to two or more drugs has proved to be not only effective but extraordinarily safe. As combination microbicides advance in preclinical testing, it will be critical to work with regulators on how best to evaluate the relative safety and effectiveness of single vs. combination approaches for use by HIV-uninfected individuals.

Need for greater coordination: The microbicide field has established multiple mechanisms for active communication and coordination to ensure that knowledge gained from past successes and failures informs future decisions. These include the Clinical Trials "Quick" Working Group and Microbicide Donors Committee, both coordinated by the Alliance for Microbicide Development. Despite the relative absence of large pharmaceutical companies from the microbicide field, new chemical entities and formulations, new models, innovative approaches to improve adherence, and more efficient trial designs are shared through these cross-coordination efforts. This is made possible by a valuable diversity of funders, including the U.S. government (CDC, NIH, USAID), U.K. Department for International Development and Medical Research Council, and philanthropies such as the Bill and Melinda Gates Foundation. Cross-agency coordinating functions recently established by the NIH Office of AIDS Research should also enhance future decision-making.

"Whither or wither microbicides?" asks the microbicide field to contemplate its past and future. Some of its recommendations are being implemented; others, such as combination strategies, are in early stages. We recognize that we must pursue only the best scientific leads; better integrate basic, behavioral, and clinical research; and leverage and deploy human and monetary resources efficiently. What we cannot do is wait. The need for effective HIV prevention methods is too great.

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