HIV TOPICAL MICROBICIDES: THE CURRENT DEVELOPMENT STRATEGY IS FULLY JUSTIFIED

In his critique of current microbicide trials, Michael Gross states: "People may die because research delays defer answers that could have spared them. People also may die because research proceeds down a blind alley or stalls progress in more promising avenues of investigation."[1(p1088)] Let us be quite clear. People *will* die—*are* dying—in very large numbers because of delays in developing microbicides. It would be unconscionable and indeed unethical to tolerate further delays if they are avoidable. We must therefore look carefully at Gross's twin contentions that the current strategy will come to nothing and that it will hinder work on the next generation of microbicides.

The trials referred to were scrutinized in April 2004 by the International Working Group on Microbicides and subsequently at the consultation mentioned by Gross. It was affirmed that they should all go ahead, with the recommendations that they be organized to ensure integrated assessment of findings and that, where necessary, protocols be

strengthened to improve safety monitoring. Mechanisms are being established to facilitate implementation of these recommendations.

Gross argues for evaluating multiple products head-to-head in a single study. The difficulties of mounting such a large and complex trial, achieving multistakeholder consensus on design, and obtaining approvals mean that a delay of several years would be inevitable, with no guarantee of success. Gross also indicates that the pharmaceutical industry's approach would be to evaluate only the most promising of the 4 different polyanion microbicides among the current products. However, while product selection in conventional drug development can draw on well-tested surrogate markers of safety and efficacy, with microbicides we will have no validated surrogate markers of either until we are able to correlate the clinical findings from these phase 3 trials with putative markers. This applies equally to in vitro indicators, animal models, and early clinical findings.

As Gross says, there are some promising new microbicides in the pipeline, but important questions must be answered about their safety, efficacy, and cost before their phase 3 evaluation would be justified. And it is so far only an assumption that they will be superior to current products. Far from posing a threat, the present work will pave the way for trials of future entities by creating site infrastructure and local expertise and by testing trial designs. It cannot fail to move the microbicide field substantially forward and may give us a product that can begin to save lives. ■

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Reference

1. Gross M. HIV topical microbicides: steer the ship or run aground. *Am J Public Health.* 2004;94: 1085–1089.