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Introduction

Trends in microbicide formulations workshop

CONRAD, a division of the Obstetrics and Gynecology Department of Eastern Virginia Medical School sponsored a workshop entitled Trends in Microbicide Formulations in Arlington, VA on 25 and 26 January 2010. Experts from the microbicide field were invited to present the latest in formulation science and technology used to optimize vaginal delivery of microbicides. Around 100 participants from research institutions, funding agencies, and foundations participated in the meeting.

The workshop was structured to address several objectives with respect to microbicide formulations. The major objective was to present the current state of microbicide formulation science including scale-up and manufacturing. Scale-up and manufacturing of microbicide products requires an understanding of current regulatory guidelines specific to developing world countries that have yet to be fully addressed in the microbicide field. Microbicide gel products have been scaled up to provide clinical supplies for Phase III trials. An intravaginal ring product capable of delivering the nonnucleoside reverse transcriptase inhibitor dapivirine is now in Phase II testing while all other dosage forms (fast dissolve films, tablets, and capsules) are in earlier stages of development. To ensure global access, cost effective manufacturing of microbicide products will be critical in their introduction into developing countries unable to support cost of goods and margins expected in the developed world.

The scientific basis for effectiveness of topically (vaginally) applied drugs, in particular, antiretroviral drugs, to prevent HIV-1 transmission was presented. These presentations are reviewed by Hladik and Doncel (2010). The preclinical evaluation of microbicides was cover in a presentation by Doncel; this presentation is reviewed by Doncel and Clark (2010). Microbicide products approaching clinical or currently in clinical evaluation are based on existing (non-microbicide-based) vaginal products (e.g., gels and intravaginal rings). To that end, presentations on vaginal gels, fast dissolve films, fast dissolve tablets, and intravaginal rings including scale-up and manufacturing/regulatory considerations are reviewed in two papers. The first by Garg et al. (2010) reviews gels, fast dissolve films, and fast dissolve tablets and the second by Malcolm et al. (2010) addresses recent advances in intravaginal rings.

Clinical evaluation (acceptability and pharmacokinetics/vaginal deployment) of novel microbicide formulations is addressed in a paper by Morrow and Hendrix (2010) based on their presentations. Another topic related to microbicides is Dual Protection (or Multipurpose Technologies). These technologies are designed to deliver two (or more) drugs to simultaneously 1) prevent the transmission of HIV-1 and -2) provide protection against unwanted pregnancies or protection against a second sexually transmitted infection (e.g., HSV-2). These topics are covered in an in-depth review (Friend and Doncel, 2010).

Clinical evaluation of microbicides products has focused on dosage forms already commercialized (e.g., gels). However, there is a need to develop newer delivery systems to address potential short comings of traditional vaginal formulations. Novel systems include nanoparticle-based vaginal delivery systems, localized delivery of peptides/protein therapeutics, and vaginal administration of anti-HIV vaccines. The safety of these and other dosage forms is of critical concern based on earlier clinical trials with microbicides (e.g., nonoxynol-9) demonstrating enhanced HIV-1 transmission rather than protection. These topics are covered in a review by Whaley et al. (2010).

At the time the workshop was conducted, no microbicide product had proven successful in several Phase III studies. The microbicide field could be characterized as *in media ras*. Since then, results of a Phase IIB trial conducted in South Africa (CAPRISA-004) using a gel product (Tenofovir 1% Gel) demonstrated significant reduction in the transmission of HIV-1 (Abdoll Karim et al., 2010). This proof of concept trial is an exceptional milestone for the microbicide field. As a result, microbicides have attained unprecedented attention. Microbicide formulations will take on increasing importance as additional studies, including combination of two or more antiretrovirals, to create marketable products available in the developing world.

The workshop was the result of many people dedicated to a common goal. I first want to thank the co-chairs, Sanjay Garg and Gustavo Doncel, in making the Workshop a success. The input of Henry Gabelnick was equally important. From CONRAD, the hard work of Ruvi Makuni, Sarah Maitz, and Anna Swanson made the Workshop logistics seamless. Finally, the Workshop could not have taken place without the generous financial support of the United States Agency for International Development.

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David R. Friend*
CONRAD, Arlington, VA 22209, United States

*Tel.: +1 703 276 3906.
E-mail address: dfriend@conrad.org

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