



Overview – Microbicide Vaginal Rings

HIV/AIDS is the leading cause of death globally in women ages 15-44, and exacts an especially high toll in sub-Saharan Africa, where the epidemic has hit hardest. Each day, more than 3,000 women are newly infected with HIV, yet women lack a discreet method that they can use to protect themselves from infection. Vaginal microbicides — products being developed to reduce the risk of HIV transmission to women during sex with an HIV-positive male partner — promise to address this central gap in current HIV-prevention strategies.

The International Partnership for Microbicides (IPM), a nonprofit product development partnership, is developing microbicides based on the same types of potent antiretroviral (ARV) drugs used successfully in HIV/AIDS treatment and in the prevention of mother-to-child transmission of HIV. Now IPM is testing a medical technology commonly used to deliver contraceptive hormones in Europe and the United States — the microbicide vaginal ring — to deliver these ARVs to help protect women from HIV in the world's most at-risk areas.

In June 2010, IPM initiated the first expanded safety study of an ARV-containing vaginal ring in Africa. While microbicides may come in many different forms, vaginal rings have tremendous promise because they could offer discreet, effective and sustained protection against HIV infection.

Microbicide Ring Technology:

Convenient and easy to use, vaginal rings are increasingly popular among women in developed countries for contraception and other medical uses. IPM is taking this device and working to adapt it in the fight against AIDS in developing countries.

Vaginal rings are designed to provide slow and controlled release of drugs into the vagina over extended periods of time. There are currently three vaginal rings approved and marketed for use: NuvaRing® (Merck) for contraception; and Estring® (Pfizer) and Femring® (Warner Chilcott) for hormonal therapy.

The ring used in IPM's clinical trial, called IPM 015, is a flexible ring made of silicone with the drug dapivirine uniformly dispersed throughout, in a design referred to as a matrix ring. The microbicide vaginal rings for this trial are being made by IPM at its manufacturing plant in Pennsylvania.



Benefits of Microbicide Rings

Vaginal rings have a number of potential benefits that could make them well-suited for microbicides. A microbicide vaginal ring could provide protection against HIV for a month or even longer. They are easy to use, discreet and have a relatively low manufacturing cost. The rings are physically stable, durable and easy to distribute, making them suitable for use in developing countries. Vaginal rings also have the potential to deliver multiple drugs in combination.

continued

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Dapivirine: The Active Ingredient

The vaginal rings being tested in IPM clinical trials contain the antiretroviral drug dapivirine. Dapivirine is being developed by IPM under a royalty-free license from Tibotec Pharmaceuticals, a subsidiary of Johnson & Johnson, for use as a microbicide in developing countries. Dapivirine has been tested in oral formulations in 11 clinical trials prior to 2004, and it has been tested in both vaginal gel and ring formulations in multiple safety trials involving more than 315 women. In all trials of dapivirine to date, it has been well-tolerated with a good safety profile.

Matrix rings have been shown to be safe and well-tolerated with low systemic drug absorption while delivering high concentrations to vaginal fluids for a month or longer.

The IPM 015 Microbicide Ring Study

IPM 015 is the first study in Africa testing the safety and acceptability of a vaginal ring containing an ARV. It is a double-blind, randomized, placebo-controlled Phase I/II safety study of a matrix ring containing 25 mg of the ARV drug dapivirine.

IPM 015 will involve approximately 280 healthy, sexually-active, HIV-negative women at multiple research centers in countries in Southern and Eastern Africa where the epidemic is hitting hardest, and women are in the greatest need of protection. Women will be randomly assigned to use either the dapivirine ring or a placebo ring (that does not contain dapivirine), for comparison purposes, and will be instructed to return to the research center and replace the ring every month for the three-month duration of the study. The study will also measure the acceptability of the ring and adherence to a product every four weeks.

Other Vaginal Ring Studies

IPM has completed four clinical studies of the dapivirine vaginal ring: IPM 001, IPM 008, IPM 018 and IPM 024. All four studies were conducted in Belgium. IPM 001 and IPM 008 were seven-day safety studies testing an earlier prototype (reservoir) ring. IPM 018 was a 28-day study comparing reservoir rings with an early matrix ring and a placebo, and IPM 024 was a safety and pharmacokinetic study of the current dapivirine matrix vaginal rings as compared to a placebo in 16 women in Belgium. In all of the studies to date, dapivirine vaginal rings were generally well-tolerated in healthy, HIV-negative women, with participants reporting no serious adverse effects. Additionally, the IPM 015 expanded safety study in Africa is underway, and the IPM 013 safety and pharmacokinetic study in Belgium is in data analysis.

Another study, IPM 011, which concluded in 2010, evaluated the safety and acceptability of vaginal rings with no active drug (placebo) in 170 women in South Africa and Tanzania. Preliminary results showed the ring to be acceptable and safe. Women had a high willingness to use the ring and high interest in discreet HIV prevention options.

Eventually, microbicides could come in many different forms, because we know from the contraceptive field that the more options women have, the more likely they are to use one of them. IPM's acceptability studies in Africa, where the need for HIV-prevention products is greatest, are designed to ensure that the vaginal ring and other potential formulations meet the needs of women living at risk of HIV.

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