



A Microbicide Ring to Protect Against HIV

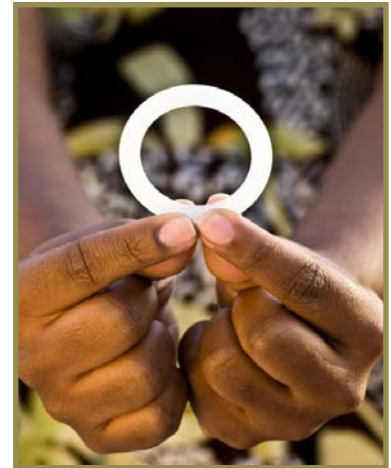
HIV/AIDS is the leading cause of death globally in women ages 15-44. It exacts an especially high toll in sub-Saharan Africa, where young women are at least twice as likely to become infected as young men. Women are particularly vulnerable to infection due to a mix of biology and social realities, and they urgently need tools they can use to protect themselves. This is where microbicides could play a vital role.

Vaginal microbicides are being developed to help prevent the transmission of HIV to women during sex with a male partner. These products may come in a variety of forms, such as a monthly ring or a gel used around the time of sex. Microbicides would address a critical gap in current HIV prevention strategies by offering female-initiated tools women could use to protect themselves from infection.

Since its launch in 2002, the International Partnership for Microbicides (IPM) has focused on developing antiretroviral (ARV)-based microbicides that contain the same types of ARV drugs already being used to successfully treat HIV/AIDS and to prevent mother-to-child transmission of HIV. Recent research shows that ARVs also hold great promise to prevent HIV.

IPM's Monthly Microbicide Ring

IPM's most advanced product is a monthly vaginal ring that slowly releases the ARV drug dapivirine. This novel product adapts a medical technology commonly used to deliver hormones to women – a vaginal ring – to the fight against HIV in developing countries, where the epidemic has hit hardest.



IPM's dapivirine ring is easy to use, and designed to remain in place for a month at a time to provide sustained protection against HIV. Given the ring's promise as a microbicide, the US National Institutes of Health-funded Microbicide Trials Network (MTN) has partnered with IPM to advance this important product in late-stage clinical trials. IPM and MTN will launch parallel clinical studies in Africa in 2012 to evaluate the ring's efficacy and long-term safety.

Benefits of the Ring

The ring has tremendous potential as a new HIV prevention method. It could offer discreet and long-acting protection against HIV. Because the monthly ring is convenient and easy-to-use, this technology may help ensure that women are able to use it consistently — a critical component of any prevention tools' effectiveness.

Efforts are underway to ensure that manufacturing costs of the ring are kept as low as possible. The low cost, along with the product's known acceptability among women and their partners, could make the ring a practical option for women in developing countries — and around the world — once it is proven safe and effective for HIV prevention.

Ring Technology

In general, vaginal rings provide slow, controlled release of drugs over extended periods of time. There are currently three rings approved and marketed for use: NuvaRing® (Merck) for contraception and Estrin® (Pfizer) and Femring® (Warner Chilcott) for hormonal therapy in post-menopausal women. IPM's microbicide ring is a novel formulation, made out of a flexible silicone material with the ARV drug dapivirine dispersed uniformly throughout in what is known as a matrix ring. In clinical studies to date, the dapivirine ring has demonstrated a good safety profile and has been well-tolerated among study populations. It has also been shown to successfully deliver the drug locally for a month or longer, with low systemic absorption.

The Active Ingredient: Dapivirine

IPM is developing dapivirine for use as a microbicide through a royalty-free licensing agreement with Janssen R&D Ireland (previously Tibotec Pharmaceuticals), one of the Janssen pharmaceutical companies of Johnson & Johnson. Dapivirine is a type of ARV drug known as a non-nucleoside reverse transcriptase inhibitor (or NNRTI), and works by preventing HIV from making copies of itself inside a healthy cell. Tibotec first tested dapivirine in oral formulations in 11 safety studies before 2004. Tibotec and IPM later tested dapivirine as a vaginal gel or ring in a total of 14 safety studies. In all clinical studies to date, dapivirine has been found safe and well-tolerated in healthy, HIV-negative women in Africa, Europe and the United States. A joint study by IPM and MTN is specifically looking at the safety and tolerance of dapivirine among men, with results expected in 2012.

The Ring: Acceptability and Safety

IPM takes women's preferences into account from the earliest stages of product development. No matter how effective a product may be at preventing HIV in a clinical study, it is essential that it fits women's needs and lifestyles so that they will use it in their daily lives to prevent HIV.

To ensure that microbicide rings meet the needs of women at greatest risk of HIV infection, IPM evaluated women's preferences as part of an acceptability and safety study of placebo rings (containing no active drug) among women in South Africa and Tanzania. Results showed the ring is acceptable to women and safe for use. Women were very willing to use the ring, and while some indicated interest in using it discreetly, the majority preferred to involve their partner. Male partners who were interviewed strongly supported use of the ring, too.

Earlier this year IPM announced results of a safety and acceptability study of the dapivirine ring conducted in four countries in Africa, which showed that the ring was safe and well-tolerated. Participants overwhelmingly found the ring acceptable to use and said they would use it if shown to be effective in preventing HIV. In addition, IPM has completed five safety studies of different formulations of the dapivirine ring in Belgium, all of which showed the ring to be safe and well-tolerated.

Next Steps: The Ring Licensure Program

In 2012, IPM will launch the dapivirine ring licensure program in Africa — the culmination of years of research demonstrating the ring's safety, acceptability, ease-of-use and long-acting duration. The full licensure program, to be conducted in collaboration with MTN, includes IPM's Ring Study (IPM 027), now underway, as well as MTN's larger ASPIRE study (MTN-020), which is set to begin in July 2012. Together, these studies are designed to evaluate the ring's ability to prevent new HIV infections in women and its long-term safety. The studies will involve thousands of women across Africa and will last approximately three years (2012-2015). The licensure program also includes several smaller studies to examine the ring's safety in adolescents and perimenopausal women, condom compatibility and possible drug interactions.

Should this package of studies show the dapivirine ring to be safe and effective, IPM will seek regulatory approval for product licensure and collaborate with key partners to help ensure the ring is made available to women in developing countries at low cost as soon as possible.

Offering Hope with New Prevention Technologies

HIV/AIDS is one of the greatest threats to women's health globally, which is why women urgently need self-initiated, practical tools to prevent infection. The monthly microbicide ring offers promising advantages, including its long-acting duration, affordability and the ability to deliver the drug where it's needed locally, with low systemic absorption. The technology has the potential to deliver combinations of ARV drugs, as well. The ring could also combine an ARV drug with a contraceptive, allowing women to simultaneously address their HIV prevention and reproductive health needs. Rings and other female-initiated HIV prevention products promise to empower women to protect their health — and, in turn, that of their families and communities.