

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 be 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 prevention strategies by offering female-initiated protection from HIV.

Since our 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 used successfully to treat HIV/AIDS and prevent mother-to-child transmission. The latest research shows that ARVs can prevent HIV in women when they are used consistently.

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 common medical technology — 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 is 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 us to advance this important product in late-stage clinical trials. IPM and MTN are both studying the ring in parallel Phase III studies in multiple countries in Africa to evaluate the ring's efficacy and long-term safety.

Benefits of the Ring

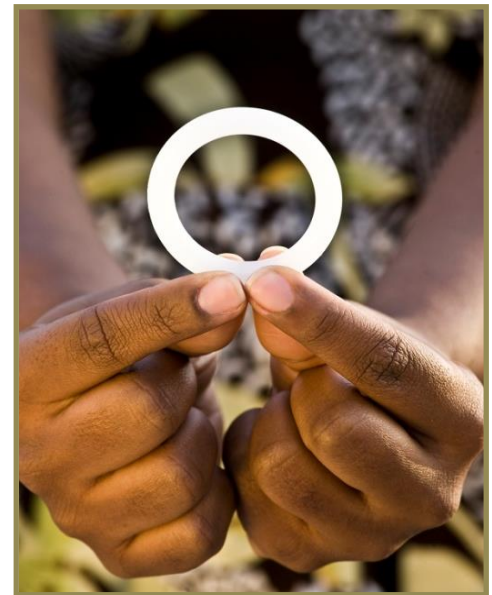
The ring has tremendous potential as a new HIV prevention method. It could offer discreet and long-acting protection against HIV. Because the monthly ring is convenient and easy-to-use, it may be easier for women to use it consistently — necessary for any prevention tools to be effective.

Efforts are underway to ensure that manufacturing costs of the ring are kept as low as possible. Affordability, 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. IPM's microbicide ring is a novel formulation. It is made out of a flexible silicone material with the ARV drug dapivirine dispersed uniformly throughout 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.

continued



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), a Janssen pharmaceutical company 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 replicating inside a healthy cell. Janssen R&D Ireland first tested dapivirine in oral formulations in 11 safety studies conducted before 2004 and later partnered with IPM, where dapivirine was tested as a vaginal gel or ring in a total of 16 safety studies. In all clinical studies to date, dapivirine has been found to be safe and well-tolerated in healthy, HIV-negative women in Africa, Europe and the United States. A joint 2012 study by IPM and MTN found the gel formulation to be acceptable to men as well.

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 it is used consistently.

To ensure that the microbicide ring would meet the needs of women who are at greatest risk of HIV, IPM conducted a study to assess the acceptability and safety of a placebo ring (containing no active drug) among women in South Africa and Tanzania. Results from this study showed that the ring is acceptable to women and nearly all women expressed an interest in using the ring if proven effective against HIV. While some indicated interest in using it discreetly, the majority of women preferred to involve their partner. Male partners who were interviewed also supported use of the ring.

The results from an additional safety and acceptability study conducted in four countries in Africa showed the dapivirine ring to be safe and well-tolerated by women in the trial. Women overwhelmingly found the ring acceptable to use and expressed interest in using it for HIV prevention. IPM has completed five additional safety studies of different ring formulations, all of which support the ring's safety and tolerability.

Now Underway: The Ring Licensure Program

IPM began the dapivirine ring licensure program in Africa in 2012 — the culmination of years of research demonstrating the ring's safety, acceptability and long-acting duration. This licensure program includes IPM's Phase III Ring Study (IPM 027) as well as MTN's Phase III ASPIRE study (MTN-020), both of which began in 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, with results expected by 2016. The program also includes several smaller studies to examine the ring's safety in adolescents and women over 45, condom functionality and possible drug interactions.

Should this package of studies show the dapivirine ring to be effective and safe for long-term use, 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.

The Ring as a Platform Technology: MPTs and Combinations

We understand that women's sexual and reproductive health needs do not exist in isolation but are an integral part of their overall health. As a result, we are applying our expertise in ring development to create a multipurpose prevention technology (MPT) that combines an ARV with a contraceptive hormone to address women's HIV prevention and reproductive health needs. This product is set to enter Phase III trials in 2015. IPM is also developing the ring to deliver multiple ARVs that target HIV at different points in its life cycle, which could potentially provide greater protection than a single drug alone.

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 is needed locally, with low systemic absorption. Rings and MPTs promise to empower women to protect their health — and, in turn, that of their families and communities.