

# A Long-Acting Ring for Women's HIV Prevention

The monthly dapivirine ring, developed by the nonprofit International Partnership for Microbicides, adapts a medical technology commonly used to deliver hormones to women—a vaginal ring—to the effort against HIV.

Despite progress against HIV/AIDS, women continue to face persistently high infection rates, particularly in sub-Saharan Africa. Women urgently need new options that meet their different prevention needs, which can also change throughout their lives.

## Offering Women Hope

IPM's monthly dapivirine ring could fill an important gap with a long-acting prevention method for women who are unable or choose not to consistently use higher-efficacy products like daily oral PrEP.

## Dapivirine Ring Research: Efficacy, Safety, Acceptability

**Efficacy:** Two Phase III studies found that the monthly dapivirine ring reduced women's risk of HIV-1 infection with no safety concerns with long-term use.

- The Ring Study, led by IPM, found that the ring reduced overall risk by 35%, and ASPIRE, led by the US National Institutes of Health-funded Microbicide Trials Network (MTN), found that the ring reduced overall risk by 27%.
- Together, the two studies evaluated monthly use of the ring in nearly 4,600 women ages 18-45 in Malawi, South Africa, Uganda and Zimbabwe.

**OLE results:** Two subsequent open-label extension (OLE) studies, DREAM and HOPE, showed increased ring use compared to the Phase IIIs, and modeling data suggested greater risk reduction—by over 50% across both OLEs. That's an encouraging trend we hope to see continue in additional planned research.

**Safety:** In addition to the Phase III and OLE studies, over 40 safety studies of different dapivirine formulations (oral treatment, gel, film and ring) support the ring's strong safety profile.

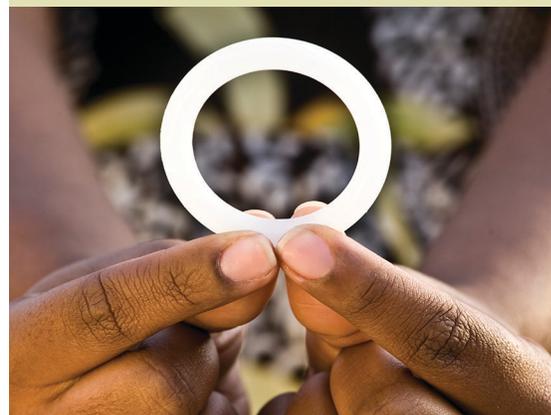
**Acceptability:** Nearly all women in two IPM acceptability studies in Africa found the ring to be acceptable and expressed interest in using it if proven effective. Many women in the Phase III studies reported forgetting the ring was in place and that neither they nor their partner could feel it during sex.

## Ring Status and Next Steps

**Regulatory:** The dapivirine ring received a positive scientific opinion in July 2020 from the European Medicines Agency (EMA) for use among women ages 18 and older in developing countries. IPM now plans to seek regulatory approvals in sub-Saharan Africa. Because many countries in Africa recognize the EMA's opinion, it can help accelerate reviews. IPM will also submit an application to the US Food and Drug Administration.

In parallel, IPM will also conduct additional research to better understand the ring's efficacy among women ages 18-25. IPM has been working across sectors to prepare for the ring's possible introduction.

**Research:** A safety study of the ring is ongoing in Africa by the MTN among adolescent girls and young women (REACH), which may support future regulatory approvals. MTN is also conducting a safety study among pregnant women (DELIVER), with a study planned for 2020 among breastfeeding women (B-PROTECTED), both in Africa, to help us understand how the ring could fit into the lives of these key groups.



INTERNATIONAL  
PARTNERSHIP FOR  
MICROBICIDES

IPM is a nonprofit organization dedicated to developing new HIV prevention technologies for women and making them available in developing countries where the epidemic has hit hardest.

## FROM CONCEPT TO RESULTS— AND BEYOND

2004

IPM obtains dapivirine license and begins preclinical work

2005–  
2010

IPM develops ring, tests four prototypes and advances one to additional clinical trials

2010–  
2012

Four early-stage studies show the ring has a strong safety profile and is acceptable to women

2012

Two Phase III studies launch in Africa

2016

Phase III studies show the dapivirine ring reduced women's HIV risk with no safety concerns

2017

First regulatory submission, ongoing research and preparations for ring rollout

2019

Two OLE studies show increased ring use and suggest greater HIV risk reduction compared to Phase III studies

2020

Monthly dapivirine ring receives positive EMA opinion

### Potential Public Health Impact

Modeling studies show that a combination approach is needed to end the epidemic—and that microbicides like the dapivirine ring could have a meaningful impact as part of it. Controlling the epidemic will require a comprehensive prevention portfolio that includes condoms, PrEP and TasP, woman-centered products like rings, and methods being developed such as injectables, implants and vaccines.

### Long-acting and Discreet

The dapivirine ring marks the first time a vaginal ring has been shown to deliver an ARV for HIV prevention. If approved, the ring would offer women the first long-acting tool they could use discreetly, on their own terms, to reduce their HIV risk.

### Ring Technology: Slow-release and locally-acting

Vaginal rings provide controlled release of drugs over extended periods of time. IPM's ring is a novel formulation made of flexible silicone with 25mg of the ARV drug dapivirine dispersed uniformly throughout its matrix (56mm outer diameter, 7.7mm cross-sectional diameter). The ring slowly delivers the drug directly to the site of potential infection over a month, with low absorption elsewhere in the body, which could help minimize side effects.

### Active Ingredient: Dapivirine

Dapivirine belongs to the same class of ARVs used to successfully treat HIV/AIDS and prevent mother-to-child transmission. Known as a non-nucleoside reverse transcriptase inhibitor, it works by blocking HIV from replicating inside a healthy cell.

### A Product of Partnership

IPM pioneered the ring's development through public-private partnerships that brought scientific ingenuity, political will and financial resources to bear at every phase of product development.

The ring got its start in 2004, when IPM obtained a royalty-free license from Janssen Pharmaceutical Companies of Johnson & Johnson to develop dapivirine as a microbicide for women. That license expanded in 2014 to an exclusive worldwide rights agreement that ensures any dapivirine product will be made available at low cost in resource-limited setting.

IPM took the ring from concept through EMA review in cooperation with governments, foundations, researchers, industry, advocates and communities. It will require that same level of collaboration to finance and coordinate the ring's introduction, where it is approved for use.

### Follow-on Products: Building on the Monthly Ring

IPM is also developing longer-acting rings that could reduce annual costs, including a three-month dapivirine ring, and a three-month ring designed to simultaneously address two risks—HIV and unintended pregnancy.