



OPTIONS

*Dapivirine Ring
Early Introduction Considerations
Seven Country Analysis*

August 2018



SUMMARY FINDINGS

DETAILED COUNTRY FINDINGS



Executive summary

THE OPPORTUNITY FOR THE RING

- Across countries, there was significant enthusiasm for the ring as a female-controlled technology that could be appropriate for adolescent girls and young women as part of a combination HIV prevention approach.
- The ring also raised questions from country stakeholders including questions on how to improve adherence among 16-24 year olds and how policies should be crafted to build the ring into a comprehensive prevention package.
- Importantly, policymakers and USAID/PEPFAR missions in most countries advised that a demonstration in each country addressing local conditions and concerns is the best way to expedite inclusion of the ring in national policies and plans. However all stakeholders emphasized the importance of linking demonstration projects to implementation – standalone demonstration projects were discouraged. This guidance is based on the experience with the introduction of oral PrEP in many countries.
- While all of the countries included in this analysis were interested in the ring, some are better positioned to be “early adopters.”
- At present, Zimbabwe and Uganda show immediate promise for a demonstration project with the ring due to national stakeholder interest and the anticipated pace of the process. South Africa and Kenya are also promising locations, though in Kenya there are still questions about how to move forward given the constraints of US funding and in South Africa stakeholders are cautious about adding new products and note that demonstrations before regulatory approval would require greater scrutiny.
- To expedite access to the ring, two steps should be pursued simultaneously over the coming year:
 1. A coordinated global effort to prepare demonstration projects in several “early adopter” countries, in close collaboration with key stakeholders and policymakers at the country level
 2. A consistent effort to communicate about the ring at the country level, especially as additional evidence is generated and the regulatory process advances

OVERVIEW OF PROCESS

- The OPTIONS (Optimizing Prevention Technology Introduction on Schedule) Consortium is a five-year, USAID funded effort to expedite and sustain access to new ARV-based HIV prevention products in sub-Saharan Africa with a focus on women and girls.
- In May 2018, seven countries (Rwanda, Uganda, Kenya, Zimbabwe, Malawi, Tanzania, and South Africa) were prioritized for analysis due to the state of the HIV epidemic in each country and experience with ring trials.
- OPTIONS conducted secondary research and interviews with key stakeholders in these countries to understand questions about the ring that could inform demonstration and processes for introducing new biomedical HIV prevention products.
- Interviews comprised a mix of policymakers, civil society representatives, donors, implementing partners, and trial contributors.



Key findings from country consultations

1

Most country stakeholders are intrigued by the ring

Country stakeholders cited female control and limited risk of creating resistance as valuable attributes of the ring. Stakeholders in Zimbabwe expressed a readiness to start a demonstration project on the ring as soon as possible. Stakeholders also had many questions about the ring (*noted on next slide*).

2

Interest in a demonstration to inform implementation

Most country stakeholders indicated a need for a local demonstration on the ring to inform policy-making and implementation planning, noting that evidence generated elsewhere would not provide the contextual detail required. Standalone projects not linked to implementation were strongly discouraged.

3

Need to leverage learnings from oral PrEP and potential to integrate the ring into roll-out in several countries

The recent experience with oral PrEP provides lessons on messaging, processes, and stakeholder engagement for the ring. Existing structures for PrEP, such as Technical Working Groups (TWGs), can also be used for the ring. The ring needs to be assessed as part of a combination prevention approach.

4

Criticality of AGYW populations across countries, and need to better understand adherence

Country stakeholders saw potential for the ring with AGYW populations that have been difficult to serve with other options, though they also requested additional evidence on how to support adherence amongst this population.

5

Thoughtful, sustained engagement process needed to introduce the ring

In many countries there is limited existing knowledge of the ring that will need to be overcome to start planning. The approval process for some countries is straightforward but each product introduction process has idiosyncrasies that need to be managed. Regular stakeholder engagement will be necessary to maintain progress.



Questions raised by policymakers

Across the seven countries, several key questions were regularly raised policymakers

ASKED BY NEARLY ALL POLICYMAKERS

Key policymakers from five out of six countries analyzed asked the following questions:

- What would be the **impact** of the ring? How many infections would be averted?
- How does the ring **fit into a comprehensive package** of prevention?***
- What is the **effectiveness of the ring in the real-world?**
- What will be the **cost of investing** in the ring?
- What are **adherence to and uptake of** the ring in the real-world?
- Which **populations** are recommended for the ring?
- What are the implications for the **health system and healthcare workers?** What additional demands will the ring place on the health system?

ASKED BY HALF OF POLICYMAKERS

Key policymakers from three out of six countries analyzed asked the following questions:

- Will the ring be **affordable** for end users?
- Has the ring been proved to be **safe?***
- To what extent does the **effectiveness of the ring differ** among various populations? Is the ring **effective among AGYW?****
- What does behavioral data demonstrate about the impact of the ring on **condom use and other reproductive health practices?**

* Questions that have been adequately demonstrated through past clinical trials







** Questions that are partially studied in the upcoming REACH study

Note: Policymakers in Kenya were not surveyed due to US government restrictions



Country readiness assessment framework

A preliminary assessment for each country is included based on six dimensions. More dimensions may be added (e.g., availability of implementing partners) as discussions progress

High-level assessment for the ring	
 HIV epidemic characteristics	<ul style="list-style-type: none">• Assesses the level of need in the country based on HIV prevalence and incidence• Specifically notes the HIV burden faced by women and girls
 HIV prevention program	<ul style="list-style-type: none">• Assesses the national HIV prevention program for comprehensiveness, inclusion of biomedical prevention, and dedicated prevention funds
 Oral PrEP experience	<ul style="list-style-type: none">• Assesses speed and ease of previous oral PrEP research, demonstration, and implementation, including inclusion in national guidelines and strategic plans
 Ring trial experience to-date	<ul style="list-style-type: none">• Highlights in-country dapivirine ring trials that could be leveraged for awareness-building and ring introduction
 Stakeholder reactions to the ring	<ul style="list-style-type: none">• Assesses knowledge, interest, and enthusiasm about the ring from a range of stakeholders including government, civil society, and academia
 Product introduction process	<ul style="list-style-type: none">• Assesses clarity and speed of typical product introduction process



Cross-country assessment for ring potential

	ZIMBABWE	UGANDA	SOUTH AFRICA	KENYA	MALAWI	TANZANIA	RWANDA
HIV epidemic characteristics	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	MODERATE NEED
<i>Prevalence rate</i>	13.5%	6.5%	18.8%	4.8%	9.2%	4.7%	3.1%
<i>New infections annually</i>	40,000	52,000	270,000	53,000	36,000	55,000	7,500
<i>Incidence rate</i>	3.03	1.50	5.46	1.21	2.29	1.19	0.70
HIV prevention program	STRONG OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY
Oral PrEP experience	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	POTENTIAL LIMITATION	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY
Ring trial experience to-date	STRONG OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY	POTENTIAL LIMITATION	POTENTIAL LIMITATION
Stakeholder reactions to the ring	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY
Product introduction process	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY <i>Due to USG ban</i>	MODERATE OPPORTUNITY	POTENTIAL LIMITATION	STRONG OPPORTUNITY



Implications of findings for ring planning



GLOBAL STAKEHOLDERS

- Country stakeholder interest and questions about the ring should **be shared with global stakeholders to inform planning and prioritization.**
- Feedback from country stakeholders underscores **the need for demonstration projects** as part of the global rollout and **the importance of coordinated demonstration planning** amongst global actors.
- Supporting awareness-building about the ring and its potential within **USAID, WHO, Global Fund and their relevant missions** is a fundamental step in the introduction process as planning, financing and approval of rollout in most countries hinges on their involvement.



COUNTRY STAKEHOLDERS

- Introducing the ring through demonstration projects will require resources and may mean that the **first phase of rollout should take place in a subset of “early adopter” countries.**
- Identifying **strong implementing partners in each priority country** to steward the stakeholder engagement and planning process will be a critical first step.
- The limited existing knowledge of the ring, coupled with country stakeholders’ eagerness to engage on demonstration planning, suggests a need for thoughtful, **consistent communications and engagement of priority stakeholders** in country between now, the EMA opinion and thereafter.
- A **customized engagement approach for different types of stakeholder groups** in each country could support introduction. For example, civil society members across countries were supportive of the new option, though they have varying levels of influence on policy-making. They can be engaged to generate demand for the ring through formal or informal channels.

SUMMARY FINDINGS

DETAILED COUNTRY FINDINGS

RWANDA





Rwanda: Potential for the Ring

LATE ADOPTER due to limited awareness of the ring and modest interest among key stakeholders. However, there is interest among CSOs and the pace of product introduction can be quite quick if policymakers are enthusiastic.

Opportunities

- **Potentially rapid introduction:** The pace of introduction could **potentially be fast**, if the RBC is on board. In fact, if the government wishes to, they have a tendency to **skip pilot projects** and move straight to national roll out.
- **Few stakeholders:** The process for getting approval for demonstration projects in Rwanda seems to **involve fewer stakeholders than in other countries** (e.g., Rwanda does not have a National AIDS Commission).
- **Resonates with civil society:** Civil society actors felt that the ring would be **well-received**, particularly since it would empower women, but cited a strong need to **raise awareness**.
- **Positive legal climate:** Selling sex is **becoming decriminalized**, so there may be **less concern about moral pushback** than in other countries.
- **National HIV Strategic Plan revision:** The current National Strategic Plan (NSP) demonstrates a **strong commitment** to preventing new HIV infections. The NSP is currently being **revised**, so it is an opportune time to be discussing the ring.
- **FSW intervention:** Rwanda has a low HIV prevalence overall compared to other places, but many stakeholders cited the **sex worker prevalence of almost 50%** and believed the ring would be a useful intervention for FSW. However, the ring may not be the intervention most suitable for FSW given that efficacy remains lower than oral PrEP.

Challenges

- **Less familiarity with the ring:** Overall, there is **limited knowledge** about the product. There were many questions about whether the ring could be used as treatment, so **clear messaging** is required.
- **Moderate government support:** The key government stakeholder, Dr. Sabin Nsanzimana (RBC), wants to see more data about the **efficacy** and the **acceptability** before he is enthusiastic about the potential for the ring.
- **Less infrastructure for research:** Rwanda participated in Phase I and II dapivirine gel trials, but due to **challenges with processing lab samples** and the lab not being certified in good clinical laboratory practice (GCLP), Phase III dapivirine ring trials were not conducted in Rwanda. Lab capacities may need to be developed for further demonstration.
- **Costs:** As with other countries in the region, the **costs** of funding another HIV prevention technology is a limitation.
- **Social acceptability:** Health care providers shared that many women seem to **prefer pills or injections over insertables** (e.g., IUD) due to concerns of side effects and losing foreign objects inside the body.



Rwanda: Assessment overview

High-level assessment for the ring

A computer monitor displaying a bar chart and a pie chart.	HIV epidemic characteristics	MODERATE NEED: Overall, Rwanda has a relatively low HIV prevalence (3.1%) and 7,500 new cases per year. However, it is estimated that a majority (65%) of new infections are among serodiscordant couples (SDC).
A building with a cross on top, representing a healthcare facility.	HIV prevention program	MODERATE OPPORTUNITY: FSW, AGYW, and SDC are focus populations in the national plan; however, there is limited funding for the HIV response.
A blue pill bottle with a white cross on the label.	Oral PrEP experience	MODERATE OPPORTUNITY: Rwanda has not yet included oral PrEP in national plans, but plans to include oral PrEP in the new NSP this year. An oral PrEP demonstration project may be on the horizon.
A blue circle with a white ring inside, representing a ring trial.	Ring trial experience to-date	POTENTIAL LIMITATION: Rwanda has not been involved in any phase III or OLEs for the ring. Rwanda was involved in Phase I/II but discontinued due to lab resource constraints.
Two overlapping speech bubbles, representing communication or stakeholder reactions.	Stakeholder reactions to the ring	MODERATE OPPORTUNITY: Many stakeholders were not familiar with the ring, but seemed interested in the product and saw benefits of adding an additional option to the prevention toolkit for women.
A clipboard with a checklist and a pencil, representing a process or introduction.	Product introduction process	STRONG OPPORTUNITY: The introduction process in Rwanda is straightforward and can be quite quick, but it hinges heavily on the perceptions of a few key stakeholders.

Additional details on following slides



Rwanda: HIV context

Rwanda has an estimated

222,000

people living with HIV, which accounts for

3.1% of the adult population

and

7,500 new infections

occur annually¹

Overall, Rwanda has a **low HIV prevalence** compared to other countries in the region and 67% of people living with HIV are on treatment.¹ However, **female sex workers, serodiscordant couples, youth and MSM** remain populations facing the most risk of HIV infection and the government has identified these groups as key populations of focus in the National Strategic Plan.

Women are affected more than men¹

HIV prevalence is higher for women ages 15-49 (3.8%) than for men of the same age (2.3%)

Female sex workers are disproportionately affected^{1,2}

HIV prevalence is 45.8% for sex workers. 20% of new HIV infections are projected to be from female sex workers and their networks

HIV among adults is highest in Kigali City²

HIV prevalence is higher in Kigali City (7.3%) than in the other provinces (average 2.4%)

Serodiscordant couples comprise the majority of new projected HIV infections²

The majority of new infections (65%) are projected to come from stable heterosexual relationships, including serodiscordant couples



Rwanda: HIV prevention context

Context

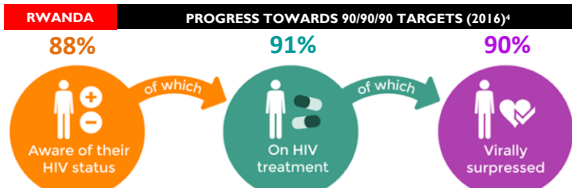
- **Political landscape:** Rwanda has seen significant gains in economic development and enactment of progressive health policies, including a near-universal health care system and declaration of health as a human right in 2003.^{6,7} Life expectancy has doubled from 35 in 1995 to 67 in 2017. Moreover, sex work may soon become decriminalized, which could improve access to health care for FSW.³ However, civil society and media activity is limited by government regulation.⁵
- **Recent progress with prevention and treatment:** Rwanda has met two of the three 90-90-90 goals: 91% of people aware of their HIV status are on HIV treatment of which 90% are virally suppressed. Awareness of HIV status is also high, at 88%.

National Policies and Strategies for Prevention

- **Four key populations:** The majority of prevention efforts are directed towards (1) FSW and their clients; (2) MSM; (3) Youth (especially young women ages 15-24); and (4) SDC
- **Wide array of prevention efforts:** Prevention efforts include promoting condoms, HCT, VMMC and newborn circumcision, post-exposure prophylaxis (PEP), wraparound support for survivors of gender-based violence, and “prevention with positives” (treatment with ART and behavior-change for PLHIV). Oral PrEP is not included but is supposed to be in the new plan^{2,3}
- **Desire to integrate HIV with SRH:** SRH/family planning is not well integrated with HIV services, and is stated as a goal^{2, 3}
- **NSP currently being renewed:** The NSP incorporates input from communities, CSOs, government, and development partners. The current NSP was for (2013-2018) and is in the process of being renewed^{2,3}

Remaining Challenges with Prevention

- **Inconsistent condom use during high risk sex:** Condom use at last high-risk sex for adults ages 15-49 was 54.7%¹ The NSP reported limited accessibility of condoms at community level as a challenge for the prevention program²
- **Low percentage of men are circumcised:** 29.6% of men ages 15-49 are circumcised¹
- **High rate of intimate partner violence:** In 2010, 44.3% of Rwandan women ages 15-49 have experienced recent intimate partner violence¹
- **Low knowledge of HIV prevention among youth:** Only 51% of young people (ages 15-24) are knowledgeable about HIV prevention¹
- **Decreased funding for the HIV response:** The NSP highlights that “the difficult international financial environment has affected HIV funding internationally and Rwanda is no exception to this”²
- **Barriers to access:** FSW and MSM face particular barriers to access including discrimination and stigma²



Sources: (1) <http://www.unaids.org/en/regionscountries/countries/rwanda> (2) National Strategic Plan on HIV and AIDS 2013-2018 (3) FSG interviews (4) Graphic from AVERT (modified by FSG); Data: UNAIDS special analysis 2017 (5) Human Rights Watch World Report 2018: Rwanda Events of 2017 (6) Universal health coverage in Rwanda: a report of innovations to increase enrolment in community-based health insurance, Makaka, Andrew et al., The Lancet, Volume 380, S7 (7) The Global Fund <https://www.theglobalfund.org/en/portfolio/country/?k=a76e4125-b5f5-41c8-8bcc-82d9dc5d1342&loc=RWA>



Rwanda: Status of oral PrEP rollout

Oral PrEP Rollout

- **Oral PrEP is not currently in the treatment guidelines.** Resource limitations were cited as a main reason why there was pushback on oral PrEP
 - *“We had to figure out how to rationalize very few resources. Do we prefer to provide testing, buy condoms, and treat those who need treatment or spend money on prevention?”* -Civil society representative
- **Oral PrEP will likely be included in the new version of the National Strategic Plan.** The current plan ends this year, and stakeholders mentioned that oral PrEP was talked about a lot at a TWG meeting for likely inclusion in the plan
- **An oral PrEP demonstration project may be on the horizon.** Starting this October, PEPFAR may conduct a demonstration project for oral PrEP. Project San Francisco, a potential civil society implementing partner, mentioned that if a demonstration project happens, they would be an implementing partner. Despite several attempts to connect, it has been difficult to reach PEPFAR to confirm whether or not a demonstration project for oral PrEP is moving forward



Rwanda: Ring trial activity

Dapivirine Ring Trials

- Rwanda has **not been the site for any phase III or open-label extensions**. Rather, Rwanda was involved in **phase I/II studies** to assess the safety of dapivirine gel from 2009-2011.
- IPM colleagues shared that Rwanda was not included in the phase III studies because of **complications with processing of lab samples** and **good clinical laboratory practice (GCLP) certification**

Study	Phase	Results	Partners
Phase I/II (ages 18-40) IPM 003	I/II	Microbicide dapivirine was found to be safe and acceptable ²	<ul style="list-style-type: none">• Led by: International Partnership for Microbicides• Site: Project Ubuzima• Site Investigator: Gilles Ndayisaba
Phase I/II (ages 18-40) IPM 014A	I/II	Microbicide dapivirine was found to be safe and acceptable ²	<ul style="list-style-type: none">• Led by: International Partnership for Microbicides• Site: Project Ubuzima• Site Investigator: Gilles Ndayisaba



Rwanda: Impressions of the ring

Opportunities

“From what I’m seeing, it will be **well received**. Especially for key pops it will be useful. **Women’s control** is important. This will be a good product to **empower women**.”

– Civil society representative

“If a person is resistant to condom use they may be reluctant to use a pill. I think the ring presents **many advantages compared to oral PrEP**. There are many FSWs whose **clients don’t want to use condoms**.”

– Civil society representative

“HIV is chronic and treatment is very expensive, so I am an **advocate for HIV prevention**. We are not going to forget the treatment but we **need to put all our efforts into prevention**. If there is something like the ring that can help women, that would be a very good idea.”

– Donor

“The National HIV Strategic Plan is **being revised**. This would be the most appropriate place to put the ring in.”

– Civil society representative

Challenges

“I personally think that people should be given options, but we have to consider those **options come with a cost and who should cover that cost?**”

– Civil society representative

“A lady may feel comfortable with the ring but if the husband is not comfortable, the **husband may complain** just from knowing it’s there even if he can’t feel it.” – Donor

“I haven’t been so excited about the ring. Clients **fear external devices** entering their body. There is a fear of it getting **lost** inside and of **side effects**. Women prefer pills or injections compared to something that is inside the body.”

– Policymaker

“**Treatment is the first priority**. Once someone is suppressed HIV is harder to transmit. We are focusing on those who are affected to suppress and then on prevention.”

– Civil society representative



Rwanda: Key questions about the ring

- 1 To what extent does ring **efficacy increase** during a demonstration project?
- 2 How do Rwandan women view the ring? Is **acceptability** higher than it was for other ring products?
- 3 How does **sexual behavior** change as a result of dapivirine ring use?
- 4 What is the **cost** of the dapivirine ring and what is the **cost/benefit** analysis compared to other prevention options and HIV/AIDS treatment?
- 5 How can **harder-to-reach populations** (e.g., FSW and “VIP sex workers”) gain access to the ring? Will they be available at health posts or kiosks? Is it possible to make the ring **available without a prescription**?



Rwanda: Interviews

Polymakers

1. Dr. Sabin Nsanzimana, Director of the HIV program, HIV/AIDS, STIs and Other Blood Bone Infection Division of the Rwanda Biomedical Center

Civil Society

4. Wandera Gihana Manasseh, Executive Director, Society for Family Health (SFH)
5. Dr. Aflodis Kagaba, Executive Director, Health Development Initiative (HDI)
6. Cat Kirk, Director of Maternal and Child Health, Partners in Health (PIH)
7. Dr. Karita Etienne, Country Director, Project San Francisco (PSF)
8. Dr. Alfred Twagiramungu, Jhpiego
9. Dr. Eugene Rugwizangoga, Technical Advisor, Jhpiego
10. Michelle Marie Umulisa, Rinda Ubuzima and Partners in Health
11. Sage Semafara, Executive Secretary, R.R.P+ Rwanda Network of People Living with HIV/AIDS

International Donors / Partners

12. Dr. Jules Mugabo, HIV, STIs, Hepatitis and Tuberculosis Programmes, WHO