



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.



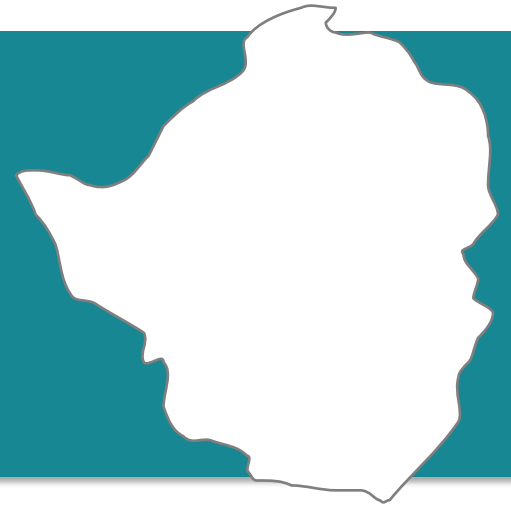
COUNTRY STAKEHOLDERS

- 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

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ZIMBABWE





Zimbabwe: Potential for the ring

EARLY ADOPTER due to high interest from the MoHCC to include the ring as part of combination prevention, a perceived opportunity to strengthen women's power and agency, and the possibility to merge ring into oral PrEP roll out.

Opportunities

- **Strong knowledge and enthusiasm:** Most stakeholders were aware of the ring, and were enthusiastic about potential introduction.
- **Technical advantages:** Stakeholders across sectors favored that the ring is women-controlled, only requires monthly action, and represents another option for women, particularly AGYW.
- **Strong interest from policymakers:** The MoHCC seemed very eager to advance to a demonstration project in Zimbabwe. Additionally, policymakers did not regard ring's partial efficacy as a barrier, believing some protection is better than none: *"one HIV infection is one too many."*
- **Build from oral PrEP's groundwork:** Stakeholders believe they will be able to build on the existing national guidelines for oral PrEP and will also be able to extend the remit of the PrEP Technical Working Group to include the ring.

Challenges

- **Funding:** The primary challenge in Zimbabwe is funding. Oral PrEP has struggled with funding shortfalls, and securing commitments from donors will be necessary before demonstration.
- **Limited coordination among civil society:** Apart from PZAT, national civil society organizations are limited in their coordination with one another. This could be a challenge to meaningfully and efficiently engage with civil society.
- **Urgency for quick action:** Researchers and other stakeholders involved in the open-label extensions are eager to see very quick action to make the ring available for OLE (open label extension) participants as soon as possible. There may be some pressure to move very quickly in Zimbabwe.



Zimbabwe: Assessment overview

High-level assessment for the ring

A computer monitor displaying a bar chart and a pie chart.	HIV epidemic characteristics	SIGNIFICANT NEED: Zimbabwe has a particularly high prevalence rate at 13.5% and experiences 40,000 additional infections annually. Women face greater risk for infection.
A building with a cross on top, representing a healthcare facility.	HIV prevention program	STRONG OPPORTUNITY: Zimbabwe has created a leading combination prevention program, and has quickly adopted and effectively implemented a range of prevention approaches.
A small bottle with a cross on it, representing a medicine or pill.	Oral PrEP experience	STRONG OPPORTUNITY: While it took over two years to develop a PrEP implementation plan, Zimbabwe has now enrolled over 5k people on PrEP. This experience can be applied to ring introduction.
A simple blue circle.	Ring trial experience to-date	STRONG OPPORTUNITY: Zimbabwe was included in phase III / OLE, and is a study site for REACH. Stakeholders have strong knowledge of the ring.
Two overlapping speech bubbles, representing communication or reactions.	Stakeholder reactions to the ring	STRONG OPPORTUNITY: All stakeholders were enthusiastic about a women controlled product. In particular, the MoHCC was eager and seemed confident in next steps.
A clipboard with a checklist and a pencil, representing a process or plan.	Product introduction process	STRONG OPPORTUNITY: Zimbabwe has developed clear steps for introduction, and will likely be able to start demonstration earlier than other countries.

Additional details on following slides



Zimbabwe: HIV context

Zimbabwe has an estimated

1.3 million

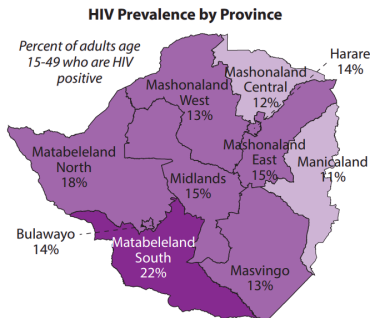
people living with HIV, which accounts for

13.5% of the adult population

and

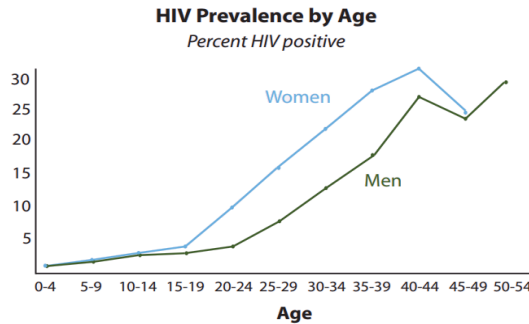
40,000 new infections

occur annually ¹



Darker purple signifies higher prevalence

Women are disproportionately affected at all ages ²



This is particularly true for young women, as **women ages 23-24 have a prevalence of ~14%**, compared to 6% for men the same age ²

Additionally, **~8,600 boys and 14,800 girls** between the ages of 15-24 years are **newly infected** with HIV each year ³

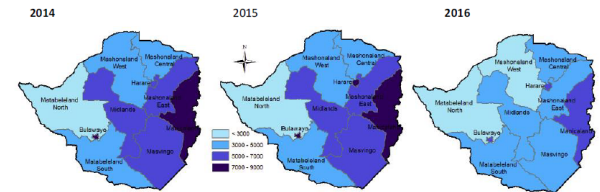
Sex workers are at much higher risk for infection ³

Sex workers and their clients account for an **estimated 12% of new infections**, and HIV prevalence among sex workers is **~60%**

A majority of new infections are among serodiscordant couples ³

Heterosexual people in stable unions or people considered to engage in “low risk” heterosexual sex account for **~54.8% of all new infections**

Southwestern provinces have higher prevalence, yet eastern provinces face higher incidence ^{2, 3}



Darker blue signifies greater incidence



Zimbabwe: HIV prevention context

Context

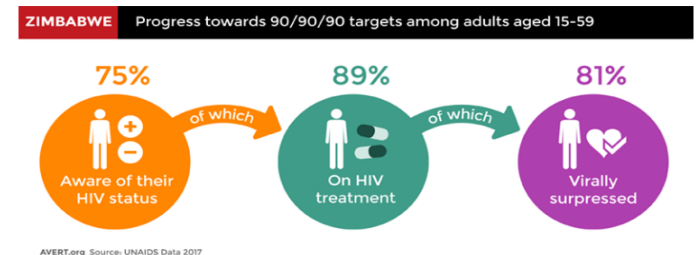
- **Political landscape:** Zimbabwe is regarded in the region as a **leader in adopting new approaches**, and the political landscape in Zimbabwe is the most favorable for the ring among all seven countries. Policymakers are eager to start a demonstration project on the ring, the process to do so is quick, and there is commitment to proceed with implementation when the results are promising.
- **Recent progress with prevention and treatment:** Zimbabwe has made **considerable progress** to address the HIV epidemic through investments in **combination prevention** targeted toward **high risk populations** and investments ensuring **full treatment and care access**. Zimbabwe has decreased annual new infections from **79,000** in 2010 to **40,000** in 2016. ^{1,2}

National Policies and Strategies for Prevention ¹

- The prevention strategy focuses on combination prevention, integrating **biomedical, behavioral, and structural** responses. Core programs include HIV Testing & Counseling, Behavior Change & Demand Creation, eMTCT, Condom Promotion, Prevention among Positives, VMMC and self-testing.
- Zimbabwe's response **targets the highest risk groups**, which are categorized as: children, adolescents, young people, AGYW, key populations and women. Zimbabwe also **targets geographic areas** that are most burdened.
- The **Zimbabwe National HIV and AIDS Strategic Plan (ZNASP)** is released every three years. The most recent and third version was released for 2015-2018. The ZNASP is published by National AIDS Council (NAC) in close partnership with MoHCC.
- **Budget:** Prevention accounts for over **30%** of the 2018 **\$237.6M** Strategic Plan budget. Funding has been a challenge for implementing the NSP and scaling up oral PrEP.

Remaining Challenges with Prevention

- **Legal and policy barriers:** Sex work and sex between people of the same sex are both considered illegal. Additionally, it's prohibited to promote condoms in schools. While there are not legal frameworks for prevention interventions among KPs, partners have developed routes to reach KPs. CeSHHAR in particular has developed a successful program for FSW. ¹
- **Gender norms and practices:** Despite legislation aimed at gender equity, over 27% of Zimbabwean woman have experienced sexual violence. ¹
- **Data gaps:** data gaps exist generally and particularly for KPs.





Zimbabwe: Status of oral PrEP rollout

Oral PrEP Rollout

- Oral PrEP is currently in **early implementation** stages. There are an estimated **5,000** current oral PrEP users in Zimbabwe, as of May 2018.²
- Introducing oral PrEP in Zimbabwe began with an impressive start with **developing demonstrations**, coupled with a **strong political commitment** from key decision makers. However, **insufficient funding** has led to **slow national roll out** as oral PrEP introduction has continued.²
- Zimbabwe was the site of **clinical trials, open-label extensions, implementation projects, large-scale implementation initiatives**, and **product introduction / support projects** for oral PrEP.¹
- Both Gilead's Truvada (TDF/FTC) and generic versions of TDF/FTC are **approved for prevention**.¹
- The policy, planning and funding of oral PrEP was a highly consultative process led by the PrEP TWG, chaired by the MoHCC. While this process took ~2 years, it resulted in a comprehensive, actionable **PrEP implementation plan**. However, there has been insufficient funding to sustain the implementation plan. Zimbabwe received a grant from the Global Fund, but it was not sufficient to follow through with the whole PrEP plan.
- The oral PrEP guidelines in Zimbabwe recommend that oral PrEP be offered as an additional prevention choice for **individuals at substantial risk of HIV infection** as part of combination prevention approaches. Individual risk assessments dictate which individuals are at substantial risk, but **oral PrEP is available for key and target populations, including AGYW**.¹



Zimbabwe: Ring trial activity

Zimbabwe has been the site of the **phase III ASPIRE ring trial**, and the **open-label extension HOPE**. Zimbabwe is also a trial site in upcoming **REACH Study**, which is expected to launch this year and explore acceptability and adherence to oral PrEP and the ring among AGYW.

Study	Phase	Results	Partners
ASPIRE (ages 18-45) MTN-020	III	The ring reduced risk of HIV-1 infection by ~27% overall compared to a placebo. HIV risk was cut by 56% in women older than 21, who appeared to use the ring most consistently	<ul style="list-style-type: none">• Led by: Microbicide Trials Network (MTN)• Funding: US NIH, US NIMH, US National Institute of Allergy and Infectious Disease (IND Sponsor: IPM)
HOPE (ages 18-45) MTN-025	IIIb OLE	(Preliminary) Risk reduced by ~54%	<ul style="list-style-type: none">• Led by: MTN• Funding: US NIH, US NIMH, US National Institute of Allergy and Infectious Disease (IND Sponsor: IPM)
REACH (ages 16-21) MTN-034	OLE	(Pending) Will collect safety and adherence data over the course of study product use for young women. Will also examine the acceptability of the study products. (6mo ring, 6mo oral PrEP, then choose for 6 mo)	<ul style="list-style-type: none">• Led by: MTN• Funding: US NIH, US NIMH, US NIAID, US NICHD• Sponsors: IPM, Gilead Sciences, Inc.

- **26%** of women enrolled in ASPIRE and HOPE were in Zimbabwe, across three sites: Chitungwiza-Seke South, Chitungwiza-Zengeza, and Harare-Spilhaus.
- **Key contacts** in Zimbabwe include Dr. Nyaradzo Mgodhi and Dr. Felix Mhlanga.



Zimbabwe: Impressions of the ring

Opportunities

“Donors want evidence. Start preparing programs that show that it makes sense and is worth investing in. Once the guidance comes out, **we can do this within 12 -18 months.**” – Policymaker

“We did well with family planning; women were empowered. We **really look forward to the success of the ring.** We are just waiting for one of those big announcements from WHO, UNAIDS or FDA.”
– Senior policymaker

“I am supportive because we need to **provide access to female controlled methods.** AGYW face gender-based violence, power imbalances, difficulty negotiating condom use, etc., so it’s important to have different options to find a prevention method that works for AGYW.” – International donor

“One thing we are seeing with oral PrEP is that some people want a product that doesn’t require daily use. **We need to give people options,** some may prefer a pill, but others a ring.” – Implementation partner

“HIV is a **highly feminized epidemic,** so we’ve always wanted a female initiated method to empower women. We look forward the ring – we needed it yesterday! When you invest in a woman you invest in the nation.” – Policymaker

Challenges

“Challenges may come up related to its design – **are AGYW comfortable using such a method?**” – International donor

“Introducing the ring will be a challenge – **there will be so many questions.** Decision makers will ask about efficacy, safety, cost, sustaining it, and who to target. End users will ask about side-effects, and **there will likely be myths as there was with IUDs.**”
– Implementation partner

“It’s **unclear who would be targeted** with the ring. Due to issues of adherence, it’s not very effective among women aged 18-22, so I assume we would target older. At 30%, **the efficacy is also a bit low,** which may cause some reservations.” – Implementation partner

“There is **little capacity among local civil society,** and they may be less aware of the ring. Local civil society is not at the forefront of PrEP discussions, and they don’t have access to information. There would need to be a way to keep them better informed.” – Research partner



Zimbabwe: Key questions about the ring

- 1 How does the ring fit into a **comprehensive package of prevention**? Which **populations** are recommended for the ring?
- 2 How **feasible is delivery** of the ring? What are implications for the **health system** (e.g., training needs, care delivery level, and delivery channel)? What are **costs to end users** and what is their **willingness to pay**?
- 3 How **acceptable** is the ring among AGYW? Can **partners feel** the ring? What are the **periods of risk** when using the ring?
- 4 To what extent do **young women adhere** in a real-world setting? What **impacts** adherence (e.g., clinical setting, socio-economic status), especially for AGYW?
- 5 What is the **impact of the ring**? To what extent will the ring **reduce HIV incidence**? What is the rate of **seroconversion**? Is there risk of **resistance**?
- 6 Should ring **clinical guidelines** be the same as those for oral PrEP (e.g., risk assessment, STI/HIV testing frequency)?

In addition to questions that will need to be answered in demonstration, stakeholders raised the following **technical questions** that will need to be **answered now** and have **clear messaging** during introduction:

- How long before sex does the ring need to be in? How long after sex does the ring need to stay in?
- Is ring compatible with an IUD?
- Could ring be used for post-abortion care? Post-partum?
- Should testing be every 3 months or more frequent because ring is not systemic?



Zimbabwe: Interviews

Polymakers

1. Dr. Owen Mugurungi, Ministry Of Health and Child Care, Director, AIDS and TB Programme

Civil Society

2. Chamunorwa Mashoko, Advocacy Core Team (ACT)
3. Taurayi Nyandoro, Zimbabwe AIDS Network (ZAN)
4. Definate Nhamo, PZAT
5. Imelda Mahaka, PZAT

Researchers

6. Dr. Nyaradzo Mgodzi, University of Zimbabwe – College of Health Sciences (UZ-CHS)

International Donors and Implementing Partners

7. Dr. Emily Gwavava, Population Services International Zimbabwe (PSI/Z)
8. Dr. Paul Ndebele, Medical Research Council of Zimbabwe (MRCZ)
9. Yemurai Mangwendeza/Abaden Svosvi, Clinton Health Access Initiative (CHAI)
10. Tendayi Mharadze, CeSHHAR
11. Dr. Moses Macheke, Zimbabwe National Family Planning Council (ZNFPC)
12. Mrs Tsitsi Musvosvi, Zimbabwe National Family Planning Council (ZNFPC)
13. Natalie Kruse-Levy, USAID