Zimbabwe Stakeholder Consultation Summary and Key Comments

D2D Pillar 3
1 November 2022

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MATRIX
Advancing R&D of Innovative
HIV Prevention Products for Women

The Zimbabwe Consultation

- Took place in Harare, 18-19 October 2022
- Attracted 68 participants, with 59 external stakeholders, including:
  - Medicines Control Authority of Zimbabwe
  - Ministry of Health and Child Care
  - National AIDS Council
  - Zimbabwe National Family Planning Council
  - Medical Research Council of Zimbabwe
  - Research Council of Zimbabwe
  - Representatives of WHO, CHAI, CDC
  - Former trial participants
  - Site community staff and Community Advisory Board (CAB) members
  - Young women advocates, including a member if the MOSAIC NextGen Squad
  - Civil Society
  - Healthcare providers
  - PEPFAR implementing partners

MATRIX

Meeting Objectives

1. Introduce MATRIX and describe its rationale and approach for accelerating early research and development of innovative HIV prevention products for women.
2. Sensitize stakeholders regarding early phase trials, including first-in-human studies, being conducted in Eastern and sub-Saharan Africa and discuss ways to mitigate potential community concerns.
3. Seek stakeholders' feedback on the MATRIX product pipeline
4. Establish a foundation for ongoing, bi-directional engagement through the lifecycle of the project and the product development lifecycle.

"We want you to be co-designers in this process."

(Nyaradzo Mgodi)

Agenda: Interactive Sessions and Deep Dives

- Overviews of the current HIV prevention landscape, MATRIX, the R&D process and what's involved in conducting early phase studies were followed by interactive sessions and deep dives
- Interactive sessions made use of polling software* to seek views regarding:
  - The need for additional HIV prevention options (besides oral PrEP, dapivirine ring and CAB-LA)
  - Different product classes (e.g., on-demand, MPTs)
  - The overall MATRIX pipeline
  - The notion of conducting early phase studies in SSA
- Deeper dives into:
  - TAF-EVG fast-dissolving insert and MATRIX-001
  - Monthly dapivirine vaginal film and MATRIX-002
  - MPT vaginal ring (LAMP-IVR)

* Due to technical difficulties with the Audience Response System (ARS) software, we converted all questions into a web-based platform called Mentimeter.

Is there a place for new methods and product formulations?

Polling results and sentiments expressed during the meeting

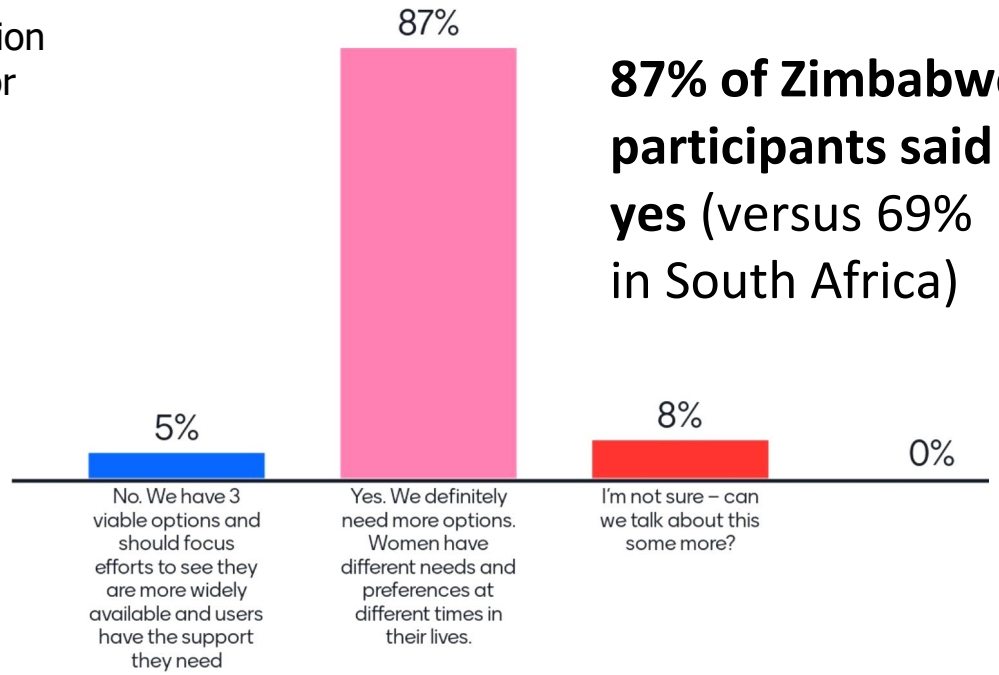
Are other options needed?

Daily oral PrEP, the monthly dapivirine vaginal ring and long-acting injectable cabotegravir are biomedical HIV prevention methods that have been approved and/or are under regulatory review in several countries. Are other options needed?

A. No. We have three viable options, and we should be focusing our efforts on seeing that they are made more widely available and ensuring counseling programs are in place to support their effective use

B. Yes. We definitely need more options. Women have different needs and preferences at different times in their lives.

C. I'm not sure – can we talk about this some more?



87% of Zimbabwe participants said yes (versus 69% in South Africa)

Are other options needed?

"It is important to have many products to ensure everyone has a product they can use. Young people are not homogenous, they have different needs."

(Young woman advocate and member of MOSAIC's NextGen Squad)

"Zimbabwe has increased the number of interventions in our tool basket but there is room for more…." Of the 32,000 taking on oral PrEP from January to June of this year, we have seen that "a third discontinue…Why? Is it because of lower risk? No. There are other factors, including unwillingness to take a daily pill…"

(Senior official, Ministry of Health and Child Care)

OF NOTE:

Early into the meeting, the Chief Regulatory Officer for the Medicines Control Authority of Zimbabwe (MCAZ) announced publicly for the first time MCAZ's approval of CAB-LA.

MATRIX

What about on-demand products?

What are your views regarding on-demand products for HIV prevention?

A. These kinds of products would be good for women who are only having sex occasionally and are likely to be preferred over a method needing to be used daily or that is long-acting.

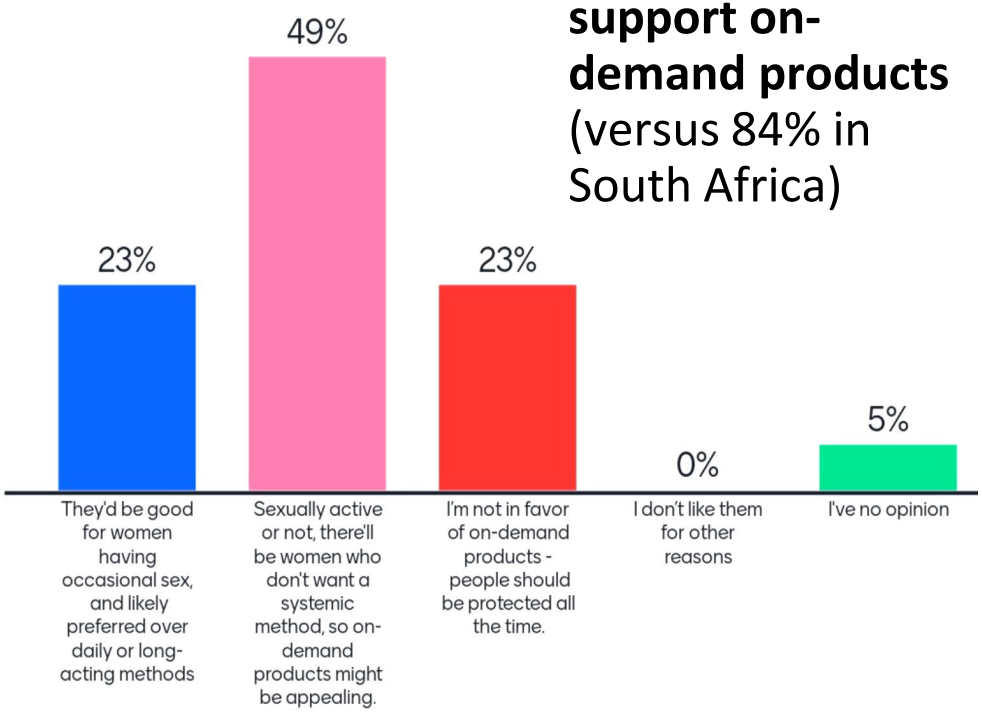
B. Sexually active or not, there will be women who prefer not to use a systemic method, so an on-demand product might be an appealing option.

C. I'm not in favor of these so-called on-demand products because everyone should have protection all the time.

D. I'm not supportive of on-demand products for other reasons.

E. I have no opinion one way or another.

72% of Zimbabwe participants support on-demand products (versus 84% in South Africa)



What about on-demand products?

- Participants who voted in the minority said they were not in favor of on-demand products because sex is more often than not spontaneous and unplanned

> *This means that "one has to do a lot of thinking on whether you are having sex or not, a lot of planning needed, but sex is most times unpredictable, spontaneous."*
>
> (Representative from THRU-ZIM – The Health Research Unit Zimbabwe, Biomedical Research and Training Institute)

> *"Sometimes sex is unpredictable, spontaneous, so on-demand products may not work."*
>
> (WHO representative)

How long should an on-demand product provide protection against HIV?

A. 2 - 4 hours

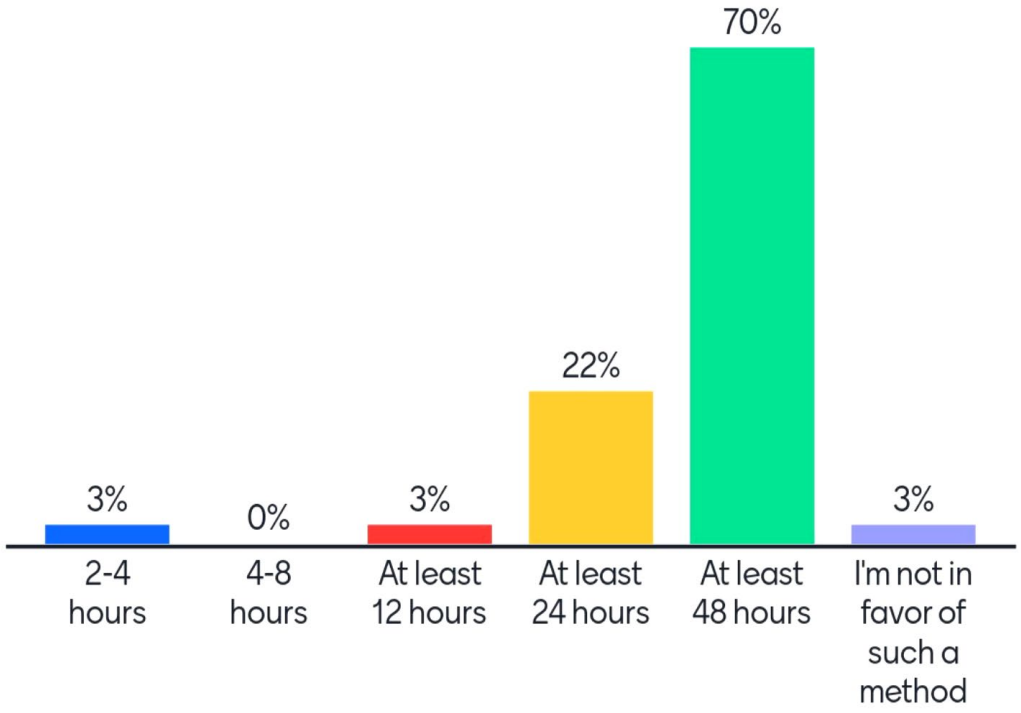
B. 4 - 8 hours

C. At least 12 hours

D. At least 24 hours

E. At least 48 hours

F. I'm not in favor of such a method



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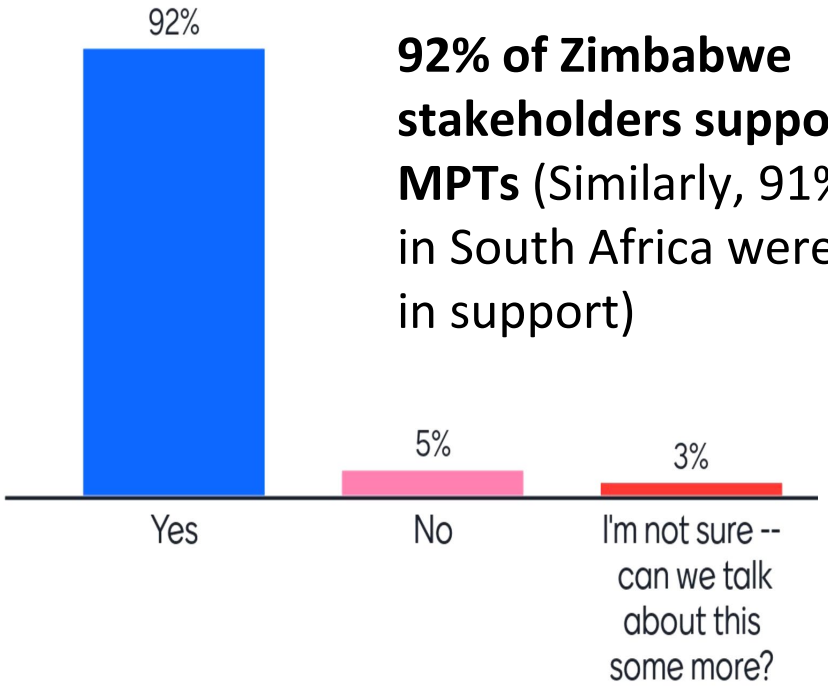
Should MPTs be a priority?

Six of the nine products in the MATRIX pipeline are being designed to not only protect against HIV but also against other sexually transmitted infections (herpes simplex virus – HSV; and/or human papillomavirus - HPV) and/or unwanted pregnancy – products often referred to as an MPT, short for multi-purpose technology. What is your opinion about MPTs – should their development be a priority for the HIV prevention field?

A. Yes
B. No
C. I'm not sure – can we talk about this some more?



92% of Zimbabwe stakeholders support MPTs (Similarly, 91% in South Africa were in support)

MATRIX

Should MPTs be a priority?

"What we really want is multiple protection and dual protection …"

(National AIDS Council representative)

"These products are really exciting because combination prevention is needed. Trying to give someone one product for HIV, another for HPV, it's a lot."

(Centre for Sexual Health and HIV/AIDS Research - CeSHHAR - representative)

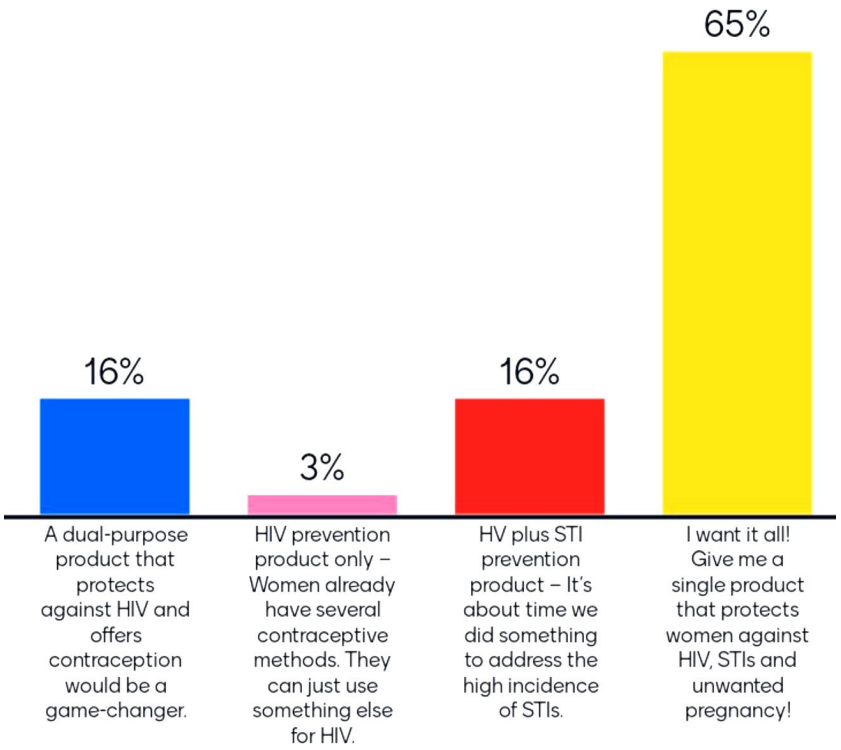
What's more important: Having an HIV prevention product that includes contraception, an HIV prevention product that protects against other STIs or a product that is solely for HIV prevention?

A. A dual-purpose product that protects against HIV and offers contraception would be a game-changer.

B. HIV prevention product only – Women already have a number of contraceptive methods to choose from. Why can't they continue with what they're already using and just use something else for HIV?

C. HV plus STI prevention product – It's about time we did something to address the high incidence of STIs. I'm all for an HIV prevention method that would work against HPV and/or HSV as well.

D. I want it all! Give me a single product that protects women against HIV, STIs and unwanted pregnancy!



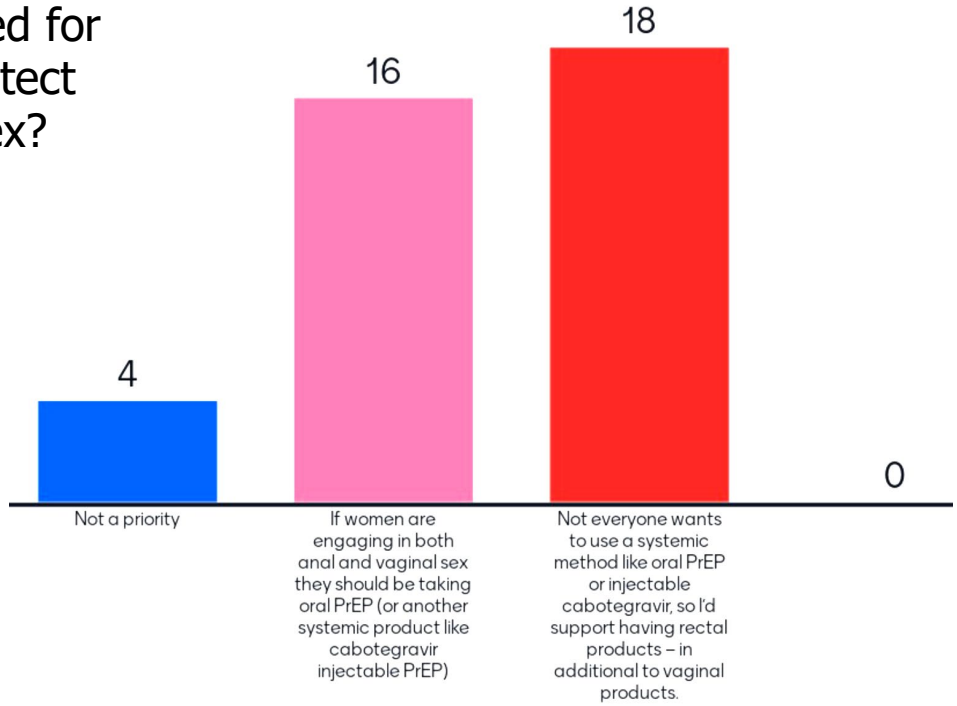
Rectal microbicides for women?

The risk of acquiring HIV through anal sex is much greater than through vaginal sex. What are your thoughts about the need for products that women could use to protect themselves against HIV during anal sex?

A. Not a priority

B. If women are engaging in both anal and vaginal sex they should be taking oral PrEP (or another systemic product like cabotegravir injectable PrEP)

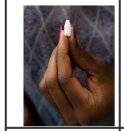
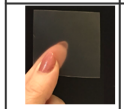
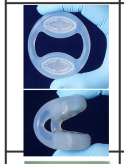
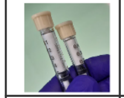
C. Not everyone wants to use a systemic method like oral PrEP or injectable cabotegravir, so I'd support having rectal products – in additional to vaginal products.

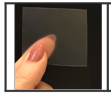


Overall MATRIX Product Pipeline

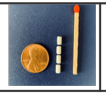
Zimbabwe Stakeholders Views

MATRIX Product Pipeline Overview

	Product	Developer	Product Type	Active ingredient	How used	How long protected?	MPT?	Unique features	Status
1	 TAF/EVG Fast-dissolving insert	CONRAD (USA)	Fast-dissolving insert	**TAF/EVG** tenofovir alafenamide & elvitegravir (NRTI and integrase inhibitor)	On-demand (at the time of sex)	Up to 3 days	HIV *and* HSV	Could be used vaginally or rectally - as PrEP or PEP	US/North American studies conducted – **first Phase 1 study in African women planned for 2023**
2	 Griffithsin Fast-dissolving vaginal insert	Population Council (USA)	Fast-dissolving insert	**A protein -Griffithsin** Viral entry inhibitor	On-demand (at the time of sex)	4 hours	HIV *and* HPV HSV	Active ingredient derived from seaweed	Pre-clinical
3	 One month dapivirine vaginal film	Univ of Pittsburgh (USA)	Vaginal film	**Dapivirine** NNRTI	Women insert themselves	1 month		Releases drug until film completely dissolves	Placebo study being planned for 2023
4	 Non-ARV/ nonhormonal contraceptive multipurpose vaginal ring	Oak Crest Inst of Science (USA)	Vaginal ring	**2 Peptides** (protein fragments) – one acts against HIV (& HSV/HPV), the other inhibits movement of sperm & ability to penetrate & fertilize egg	Women insert themselves	1-3 months	HIV *and* HPV HSV pregnancy	Non-ARV and nonhormonal Could be used with or without contraceptive	Placebo trial being planned for 2023
5	 Cabotegravir injectable depot	CONRAD (USA)	Injectable depot (storage bubble)	**Cabotegravir** Integrase strand inhibitor	Injection given under the skin	4-6 months		May be less burden on healthcare system and users	Pre-clinical
6	 Cabotegravir dissolvable pellets	CONRAD (USA)	Pellet implant	**Cabotegravir** Integrase strand inhibitor	Implanted under skin	9-12 months		Slowly dissolves over course of a year (biodegrades) Can be removed after 1-2 mo if needed	Pre-clinical

7  One month dapivirine vaginal film plus levonorgestrel (LNG)

8  Cabotegravir injectable depot plus LNG

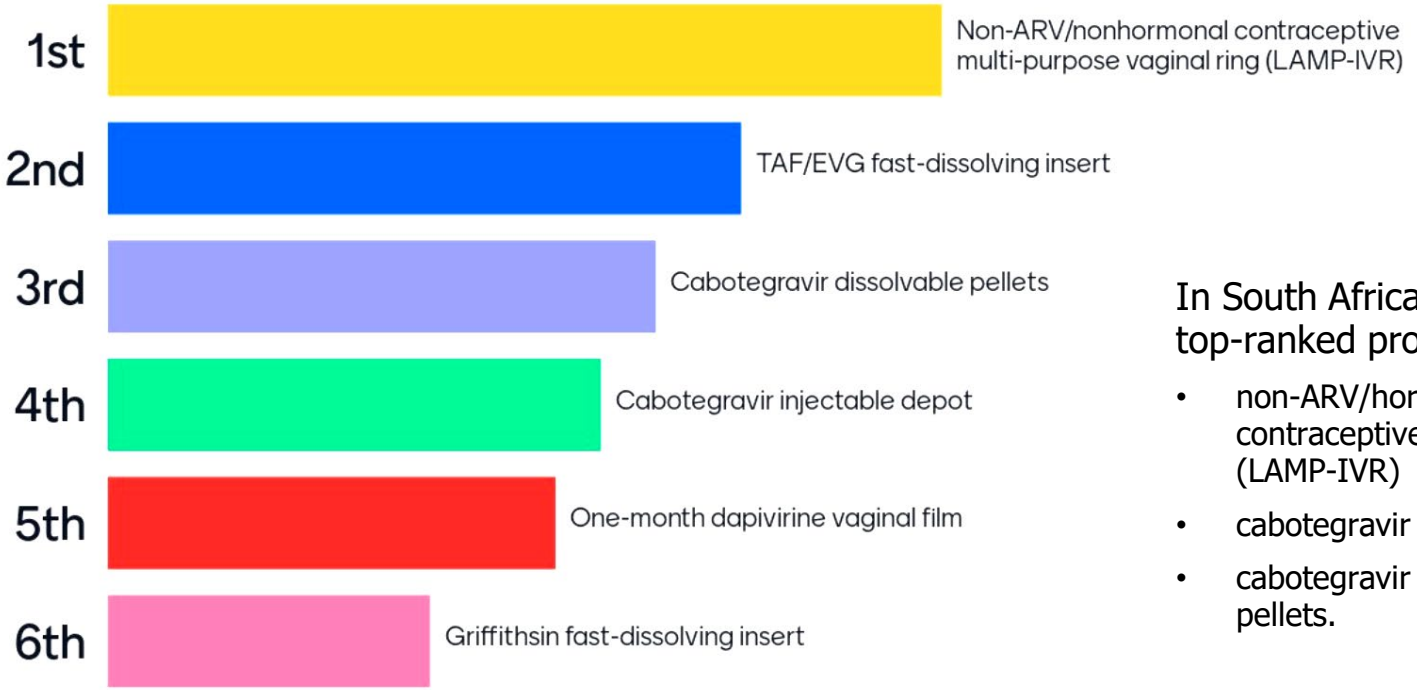
9  Cabotegravir dissolvable pellets plus LNG

Three products also to be developed as an MPT with the addition of a hormonal contraceptive

How products were presented

- All product videos were shown
  - Individual sessions were devoted to TAF-EVG fast-dissolving insert, the 30-day dapivirine vaginal film, and MPT ring (LAMP-IVR)
  - Griffithsin fast-dissolving insert and CAB dissolvable pellet implants and CAB injectable depot were featured in a session, "Looking further ahead"
- There was support of each of the products, as well as several questions (NOTE: Specific feedback about each product will be shared with individual PDs)
- At the end of the meeting, stakeholders were asked to select the 3 products they were most excited about or felt were most needed

Which 3 products in the MATRIX product pipeline are you most excited about or feel are most needed? Please rank-order your responses.



In South Africa, the three top-ranked products were:

- non-ARV/hormomal contraceptive MPT ring (LAMP-IVR)
- cabotegravir injectable depot
- cabotegravir dissolvable pellets.

"For me the least exciting is anything which requires me to visit the health facility because I would prefer options where I can just do it on my own at home."

(Behavioral Scientist and Investigator,
Harare Health and Research Consortium)

"On short-term products, we learnt during the COVID pandemic that clients using short-term FP products are at a disadvantage those clients [had] difficulties in accessing services. So this would be a minus. Also, methods that require the client to come to the facility within a month, those were at a disadvantage"

(Director Service Delivery and Training,
Zimbabwe National Family Planning Council)

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"I think it is important to appreciate that people have different tastes, different likes, one likes the film the other like the ring, another the insert, that is the way life is, we will not be able to embrace everything because there is no product with a magic bullet effect and you choose what you like"

(Advocate and Civil Society representative, Advocacy Core Team - ACT)

A need for managing expectations

- Initially, there were those who believed communities needed to be sensitized now about these products because they *"will be available within a few years*" and those concerned about overpromising at this early stage
- By the end of the meeting, stakeholders had come to realize that, indeed, not all products will make it past Phase 1, and for those that do, there will be more hurdles along the way in a process that can take up to 7-10 years – meeting participants began correcting themselves mid-sentence, using words like "*if" or "potentially" instead of "when"*
- Messaging should be congruent with where the science is

> *"In the same way we have a science pipeline, we can have a messaging pipeline … so we have messages that are contextual and appropriate for where the science stage is".*
>
> (Advocate and Civil Society representative, Advocacy Core Team - ACT)

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Views on conducting early phase clinical trials and placebo studies in SSA

Should early phase studies be conducted in SSA?

Most HIV prevention studies in Africa have been later phase studies (Phase 2 or 3) and conducted only after Phase 1 safety studies among women (at low risk of HIV) in the US or Europe indicated it be safe to do so. MATRIX intends to conduct early-phase studies here in Africa, in addition to the US. The MATRIX-001 Phase 1 study of the TAF/EVG fast-dissolving insert, for example, will enroll women at three trial sites – in the US, Kenya and South Africa. What are your views about including African women in early phase studies?

A. It's a good idea, because early safety and acceptability data from African women will result in products that African women want.

B. It's a bad idea, because safety should be assured in US women before the studies are done in African women.

C. It will be impossible to do early safety studies in African women because the women in early phase studies have to be at very low risk of HIV.

D. I'm not sure – can we talk about this some more?

75% of Zimbabwe stakeholders believe early-phase studies should be conducted in SSA (Similarly, in South Africa, it was 77%)

Feedback: Conducting early phase studies in SSA

- Involving African women is okay, if they will be prioritized as first beneficiaries of final products if and when available.
- Compensation/reimbursement for participation must be equitable across all settings – as well as the level and quality of care provided, especially if adverse events occur.

> *"A woman is the same, whether she's African or American … they have the same needs and duties [as a participant]."*
>
> (Community Advisory Board member)

- While there was much discussion on what is deemed fair and equitable reimbursement for different kinds of studies, there was also appreciation that studies should not be enrolling participants motivated by monetary or material benefit.

> *"We want people who are heroes. Money alone is and shouldn't be the only incentive. If money is what matters most, that's not the person we want for the study."*
>
> (Nyaradzo Mgodi)

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Would women participate in early-phase studies?

"I would join because I would like to be part of the trial for HIV prevention, it is good for the community"

(Former REACH study participant)

"No, I would not; I'm terrified of possible adverse effects and I'm not going to put myself out there where there's a chance of these happening."

(Young woman advocate, and member of MOSAIC's NextGen Squad)

Several stakeholders advised involving male partners and spouses as they can affect women's ability to participate in trials successfully

Views about MATRIX and its approach

"I think always getting people together, the various stakeholders from the community, from the policy makers, from the youth themselves is very important to get their views"

(Representative from THRU-ZIM – The Health Research Unit Zimbabwe, Biomedical Research and Training Institute)

"We need products that women appreciate, want to use and enjoy using. I commend the MATRIX stakeholder consultation process which was not like with the female condom, where women were not consulted on what they wanted. I am especially excited about this happening at this stage and involvement of end-users."

(Senior official, Ministry of Health and Child Care)

"The potential for local manufacturing and for over the counter– both are very exciting…"

"If we just focus on the biomedical…and not working together to address the structural issues, we'll be doing ourselves a disservice."

(Chief of Party, Zimbabwe Health Interventions)

"I think what I'm liking from a gender perspective is most of the products here are female friendly, female controlled, multipurpose, long-term and user controlled"

(Civil society representative – Zimbabwe)

From the closing remarks by the MoHCC:

> *"We know not all the products will be available – some will fall by the wayside. Messaging must be clear. But this endeavor will be helpful. Tell yourself you did well. You contributed."*
>
> (Takunda Sola, HIV Prevention and Key Populations Medical Officer, Ministry of Health and Child Care)

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Acknowledgements

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This program was made possible by the generous support of the American people through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and the U.S. Agency for International Development (USAID).

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