

MATRIX

A USAID Project to Advance the Research and Development of Innovative HIV Prevention Products for Women

2022 (Year 1)

Stakeholder Consultations in South Africa, Zimbabwe and Kenya

FINAL REPORT

January 2023



PEPFAR

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



South Africa Consultation

5-6 October 2022
Johannesburg



Zimbabwe Consultation

18-19 October 2022
Harare



Kenya Consultation

8-9 November 2022
Nairobi

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The contents of this report reflect the views and opinions of stakeholders in South Africa, Zimbabwe and Kenya and do not necessarily reflect the views of the U.S. President's Emergency Plan for AIDS Relief (PEPAR) or the U.S. Agency for International Development.

Additional information about these consultations can be found at https://www.matrix4prevention.org/research-highlights/meeting-materials-presentations-and-reports/matrix-stakeholder-consultation-reports. For more information on MATRIX and its activities, please visit www.matrix4prevention.org.

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Acronyms and Abbreviations

ARV	antiretroviral
CAB	Cabotegravir
CAB-LA	Cabotegravir long-acting injectable
CAPRISA	Centre for the AIDS Programme of Research in South Africa
HIV	Human Immuno-deficiency Virus
HHRC	Harare Health and Research Consortium
HPV	Human Papillomavirus
HSV	Herpes Simplex Virus
HSV-2	Herpes Simplex Virus -2
IEC	Independent Ethics Committee
IRB	Institutional Review Board
JKUAT	Jomo Kenyatta University of Agriculture and Technology
KEMRI	Kenya Medical Research Institute
LAMP-IVR	Luminally Acting Multi-Purpose Intra-Vaginal Ring
MATRIX	Microbicide R&D to Advance HIV Prevention Technologies through Responsive Innovation and eXcellence
MCAZ	Medicines Control Authority of Zimbabwe
MOH	Ministry of Health
MPT	Multipurpose Prevention Technology
MRCZ	Medical Research Council of Zimbabwe
MWRI	Magee-Womens Research Institute
NDOH	National Department of Health
PD	Pharmacodynamics
PEP	Post-exposure Prophylaxis
PI	Principal Investigator
PK	Pharmacokinetics
PrEP	Pre-exposure Prophylaxis
SAHPRA	South African Health Products Regulatory Authority
TAF/EVG	Tenofovir alafenamide fumarate (TAF)/elvitegravir (EVG)
USAID	United States Agency for International Development
Wits RHI	Wits Reproductive Health and HIV Institute



Executive Summary

MATRIX is a five-year (2022-2026) cooperative agreement funded by the U.S. Agency for International Development (USAID) with a mission to expedite the research and development of a range of HIV prevention products for women that beyond being safe and effective, will also be acceptable, affordable, scalable and deliverable in the settings where they are needed most. The work of MATRIX is being carried out by 19 partners from both the Global North and Global South.

A key feature of the MATRIX paradigm is its focus on being responsive to end-user and stakeholder feedback during the earliest stages of product development to inform decisions about product design and its overall research agenda. Toward this end, in 2022 – the project's first year – MATRIX convened stakeholder consultations in South Africa (5-6 October), Zimbabwe (18-19 October) and Kenya (8-9 November) to introduce MATRIX and seek stakeholders' feedback on the MATRIX pipeline of products. Consultations were attended by a wide range of stakeholders from the HIV prevention and maternal and reproductive health arenas, including policymakers, advocates, civil society, providers, regulators, ethicists, implementers, former study participants, adolescent girls and young women, other potential end-users, among others.

Each of the three meetings was guided by an agenda that was highly interactive and allowed for rich discussion. Interactive sessions made use of polling software to seek stakeholders' views regarding the need for additional HIV prevention options (besides oral PrEP, the dapivirine ring and cabotegravir long-acting injectable), such as on-demand products, which are used at or around the time of sex, and multipurpose prevention technologies (MPTs) designed to protect against HIV as well as other sexually transmitted infections (STIs) and/or unplanned pregnancy; and more specifically, to seek stakeholders' views of the products being developed under MATRIX. Meetings focused on six products, with more in-depth discussion on those closest to being evaluated in an early phase study – either as a prototype placebo (with no active agent) or of the active product itself.

Part and parcel to these discussions about the MATRIX pipeline were discussions about the realities of research and development – that it is a long process with failure typically more common than success such that very few products can be expected to make it all the way through to regulatory approval. The researchers also explained how MATRIX hopes to improve the odds for success by ensuring only the most promising products advance to early phase clinical trials – products that laboratory and animal studies suggest will be safe and effective in humans; end-users indicate they are likely to use; can be manufactured and distributed locally and at low cost; have minimal burden on healthcare systems and align with the agendas of Ministries of Health and national HIV prevention programs.

Are other HIV prevention options needed?

In Africa, daily oral PrEP is the only biomedical HIV prevention option currently available. And while the monthly dapivirine vaginal ring has been approved in several countries, it's not yet being offered, nor is long-acting injectable cabotegravir (CAB-LA) , which received its first African regulatory approval in October (2022) – in Zimbabwe – a decision announced by a representative of the Medicines Control Authority of Zimbabwe during the MATRIX consultation. Other methods in late-phase clinical trials include an injection given every six months (lenacapavir), another daily PrEP pill (emtricitabine and tenofovir alafenamide) and the dual prevention pill (which contains both oral PrEP and an oral hormonal contraceptive). A three-month dapivirine vaginal ring is also being evaluated.

As such, the first question posed to stakeholders was whether other HIV prevention methods for women are even needed. Stakeholders in all three countries made clear the answer is yes. Women have different needs and preferences at different times in their lives, and no one product can be expected to be a one-size fits all.

When asked about different classes of products, 83 percent of stakeholders supported the development of on-demand products, believing they would appeal to women not wanting to use a long-acting systemic product and women having occasional sex, though to be acceptable, such products would need to provide protection lasting at

least 48 hours. Overall, 89 percent of stakeholders also believed the development of MPTs should be prioritized. In fact, of the six MATRIX products discussed during the consultations, the non-antiretroviral (ARV), non-hormonal contraceptive MPT vaginal ring (also known as the LAMP-IVR) excited stakeholders the most[1]. There was also support for the development of products for women to protect themselves against HIV through anal sex. Notably, the majority of participants in Kenya felt that women who engage in anal sex should be taking oral PrEP (or another systemic product like CAB-LA).

What were stakeholders' views of the products being developed under MATRIX?

Stakeholders at all three consultations felt the ***TAF/EVG fast-dissolving vaginal insert***, one of two on-demand products in the MATRIX portfolio, would be an important addition to the HIV prevention toolbox, especially because it could be used as either PrEP or PEP. Its potential to protect against both HIV and herpes simplex virus (HSV) was also seen as a plus. The insert contains two anti-HIV drugs – tenofovir alafenamide (TAF), which also acts against HSV, and elvitegravir (EVG). Animal and laboratory studies suggest it would provide protection for up to three days after being inserted and could be used before or after sex and as either a vaginal or rectal product. MATRIX-001, a Phase 1 study looking at the safety and acceptability of the insert used vaginally as well as where and how the drugs are taken up in the body, will be conducted at three sites in the U.S., Kenya and South Africa in 2023 – the first study of the insert in African women. Questions about the product concerned its ease of use, how soon after insertion it dissolved and whether menstruation would be a factor.

The ***one-month dapivirine vaginal film*** is a discreet, woman-controlled method that once inserted into the vagina would slowly begin to dissolve, and in doing so, release the ARV dapivirine – the same drug contained in the monthly vaginal ring. Drug would continue to get released until the film completely disappears such that all drug would be distributed within the vagina, with nothing to discard or remove. Overall, stakeholders believed the monthly film would be an important option for women wanting longer-term and non-systemic protection, and they liked that its use could be concealed. Yet, many participants also believed it would be foreign to women, and after stakeholders themselves had the opportunity to touch and feel placebo films (with no active product), these sentiments increased. They questioned how easy it would be to insert and whether its square shape would be a deterrent to use. The MATRIX-002 study, which will assess women's use of two prototype films (containing no drug) at five trial sites in the U.S., Kenya, South Africa and Zimbabwe, will help answer many of these questions and will be the first study of a film intended to dissolve over the course of one month.

The ***non-ARV, non-hormonal contraceptive multipurpose vaginal ring (LAMP-IVR)*** generated the most interest among meeting participants because it is designed to not only protect against HIV, but also HSV and human papillomavirus (HPV), and if so desired by the user, also unplanned pregnancy for one to three months. Its active ingredient against HIV is not an ARV, which according to the researchers, would make drug resistance less of a concern should someone acquire HIV while using the ring, and because the contraceptive is not hormonally based, side effects such as irregular periods would not be anticipated. Most of the questions raised by stakeholders concerned the active ingredients, in particular the non-ARV – what is meant by a non-ARV? And if not an ARV, what is it exactly? Stakeholders felt researchers needed to be more transparent about the active ingredients contained in the ring before moving forward into possible clinical trials. While no prototype ring was available at the meetings, stakeholders' impressions were that it was too big and wondered whether it could be made smaller.

The second on-demand product in the MATRIX portfolio is the ***Griffithsin fast dissolving insert***, which contains a protein derived from red algae that acts against HIV, HSV and HPV. As currently designed, the insert would provide protection for four hours, which the majority of stakeholders felt was too short, especially given that sex is often unplanned and may take place over longer periods. Even so, there were meeting participants who thought it might appeal to women wanting protection against HIV and both HSV and HPV or preferring to use a natural

[1]Three of the six products discussed during the consultation offer protection against HIV plus HSV and/or HPV, but only the LAMP-IVR also includes a contraceptive component. Stakeholders were informed that MPT versions of three products (monthly dapivirine vaginal film, cabotegravir dissolvable pellet implants and cabotegravir injectable depot) are in their very early development, each of which would include levonorgestrel for contraception.

product. Indeed, the fact that it is based on a naturally occurring compound was intriguing and seen as potentially advantageous, yet also raised concerns, especially in South Africa, about potential misconceptions at the community level and women believing that seaweed alone would be protective against HIV.

Cabotegravir Dissolvable Pellet Implants and *Cabotegravir Injectable Depot* are products under development that contain the ARV cabotegravir, which has been found to be highly effective against HIV when given as an intramuscular long-acting injection every two months (CAB-LA). These newer formulations would potentially provide longer protection – the dissolvable pellets for up to one year, and the injectable depot for four to six months. And unlike CAB-LA, they would be delivered under the skin (subcutaneously), which would be less painful than intramuscularly, and easier and less costly to manufacture and deliver. Both products were rated high by meeting participants, yet not without a number of questions. For example, some of the younger women, having had negative experiences with contraceptive implants, questioned whether healthcare workers would have the proper skills to insert the products. And given concerns about CAB-LA's long pharmacokinetic (PK) "tail," several stakeholders wondered whether these newer products would have a similarly long tail, whereby small amounts of drug remain in the body long after use but at insufficient levels to protect against HIV, and thus, increasing the likelihood of resistance to drugs within the same class, including dolutegravir.

Should early phase clinical trials and placebo studies be conducted in sub-Saharan Africa?

Most HIV prevention studies that have taken place 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 Global North had indicated it would be safe to do so. MATRIX will be breaking new ground by conducting early phase (Phase 1) clinical trials, including first-in-human trials, and placebo studies in Africa in parallel with and in addition to those in the U.S., to gain important insights earlier in the process into the safety and acceptability of new products in the populations of women these products are primarily intended for. As such, a good portion of each consultation focused on understanding what's involved in early research and development, and in particular, the conduct of early phase studies, including studies evaluating products in humans for the first time. Stakeholders supported early phase studies being conducted in Africa and provided suggestions to help facilitate their acceptance and successful conduct. For example, because local Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs) may not be familiar with such studies, MATRIX researchers were advised to reach out to IRB/IECs in advance of submitting study protocols for review to ensure there is understanding of the rationale for these studies and why they are designed the way they are. Gaining the trust and support of male partners was also seen as important.

Not surprisingly, young women had differing opinions about whether they would consider participating in a Phase 1 study. Some said they would, to advance the science, while others were not comfortable with the potential risks involved. Stakeholders, particularly in Zimbabwe, felt study participants should receive reimbursement (compensation) commensurate with the level of commitment required of a Phase 1 study.

Conclusions

MATRIX conducted these stakeholder consultations as one of the first steps in an ongoing, iterative process to inform the early development of products, so that only the most promising products advance from pre-clinical research to early phase testing. Meeting participants were welcoming of the MATRIX paradigm, saying that all too often, drugs and other products are introduced without ever involving potential end-users, policy makers and regulators. Stakeholders also appreciated MATRIX's investment in a pipeline with a range of different products to meet women's varying needs and preferences – products that are under their control, easy to use and discreet; products that are affordable, convenient to access and require minimal or no contact with healthcare workers; and products that would not interfere with sex or daily activities. Multipurpose prevention products were especially appealing, and while methods offering longer-term protection would mean less to think about, stakeholders felt there was also a place for on-demand products. At the same time, stakeholders understood that not all of the products being developed under MATRIX would necessarily advance to Phase 1 clinical trials, and there were no guarantees of success for those that do.



South Africa Consultation



Zimbabwe Consultation



Kenya Consultation

Background and Context

In 2021, 20.6 million people in East and Southern Africa were living with HIV, and about 670,000 people in the region became newly infected (UNAIDS 2021[2]). Women and girls carry the burden of HIV infections in the region – in sub-Saharan Africa, six in seven new HIV infections among adolescents aged 15-19 years are among girls. Girls and young women aged 15-24 years are twice as likely to be living with HIV than young men.

In Africa, at present, time, only one biomedical prevention method is available—daily oral PrEP (pre-exposure prophylaxis), which requires taking an ARV tablet every day. Oral PrEP was first approved in 2012 in the U.S. and has since been approved in several countries around the globe. Today, 20 years later, the uptake of oral PrEP has not met expectations at a global level. Moreover, across all populations, including adolescent girls and young women, there is a marked decline in use after three months[3]. Clearly, not everyone finds having to take a pill every day easy.

The dapivirine vaginal ring, which is used for a month at a time, received a positive scientific opinion from the European Medicines Agency in July 2020 for its use in developing countries among women at high risk for HIV who cannot or choose not to use daily oral PrEP, and in 2021, the World Health Organization (WHO) recommended the ring as an additional prevention option for women. Despite the ring having been approved in several countries, it has not yet been made available to women. In the meantime, a study of a three-month dapivirine ring is underway.

Cabotegravir long-acting injectable, or CAB-LA, which involves receiving an intramuscular injection every two months, was approved by the U.S. Food and Drug Administration (FDA) in late 2021 and has also been recommended by WHO as an additional HIV prevention option. In mid-October (2022), Zimbabwe became the first African country to approve CAB-LA, followed by South Africa in December (2022). Approvals do not mean immediate or timely access, however, as experience has shown with the dapivirine ring, and with oral PrEP, for that matter.

Other HIV prevention options that are being evaluated in late-phase clinical trials include an injection given every six months (lenacapavir), another daily PrEP pill (emtricitabine and tenofovir alafenamide) and the dual prevention pill. Notably, all are long-acting systemic products (meaning drug is distributed throughout the body). *To learn more, visit https://www.avac.org/infographic/years-ahead-hiv-prevention-research.*

2 Global HIV & AIDS statistics — UNAIDS Fact sheet. https://www.unaids.org/en/resources/fact-sheet

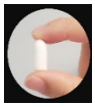
3 Rodrigues et al., Starting and staying on PrEP: a scoping review of strategies for supporting and improving effective use of PrEP, HIV R4P (2021)

About MATRIX

MATRIX is a five-year program funded in 2021 by the U.S. Agency for International Development (USAID) that aims to expedite the development of a range of safe and effective products that in addition to being safe and effective, will also be acceptable, affordable, scalable and deliverable to better meet the needs of women at risk of HIV. For instance, MATRIX is pursuing development of products that would require few or no clinic visits or not require routine HIV testing, thereby reducing the cost and burden of healthcare systems; could be manufactured and distributed locally; and importantly, that women indicate they are likely to use. MATRIX stands for Microbicide R&D to Advance HIV Prevention Technologies through Responsive Innovation and eXcellence.

MATRIX's current portfolio of products includes implants and injectables designed to protect against HIV for six months to a year; short-acting, on-demand vaginal products meant to be used around the time of vaginal sex; and other non-systemic vaginal products – meaning the drug doesn't go throughout the body – designed to provide protection for one to three months at a time. Six of the nine products are multipurpose prevention technologies (MPTs) that intend to not only protect against HIV but also other STIs (such as HSV and/ or HPV) – and/or unplanned pregnancy. Some of these products are new formulations of existing methods, while others contain novel agents. Most have yet to be evaluated in human studies. The following table shows the products in the current MATRIX portfolio.

MATRIX Product Pipeline

		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 & integrase inhibitor)*	On-demand (at 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 (MATRIX-001) planned for 2023
2		Griffithsin Fast-dissolving vaginal insert	Population Council (USA)	Fast-dissolving insert	A protein - Griffithsin *Viral entry inhibitor*	On-demand (at time of sex)	4 hours	HIV *and* HPV HSV	Active ingredient derived from seaweed/red algae	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 (MATRIX-002) being planned for 2023
4		Non-ARV/ non-hormonal contraceptive multipurpose vaginal ring (LAMP-IVR)	Oak Crest Inst of Science (USA)	Vaginal ring	A peptide *(protein fragment)- acts against HIV (& HSV/HPV)* A small molecule *Inhibits sperm's movement & ability to penetrate, fertilize eggs*	Women insert themselves	1-3 months	HIV *and* HPV HSV pregnancy	Non-ARV and non-hormonal Could be used with or without contraceptive	Placebo study (MATRIX-003) 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 a year; Can be removed after 1-2 months if needed	Pre-clinical

Three products are being developed as MPTs with the addition of a hormonal contraceptive



7 One-month dapivirine vaginal film plus levonorgestrel (LNG)



8 Cabotegravir injectable depot plus levonorgestrel (LNG)

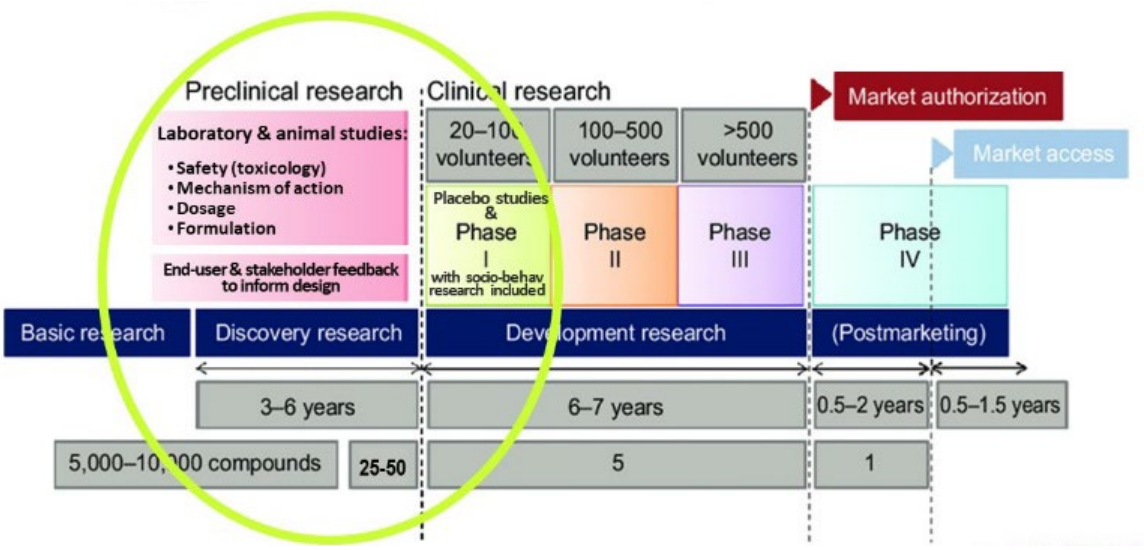


9 Cabotegravir dissolvable pellets plus levonorgestrel (LNG)

A new paradigm for conducting early research and development

MATRIX activities are focused on the early development of products, which encompasses both pre-clinical research – the laboratory and animal studies needed to support the product's evaluation in humans – and those first studies of the product, which are called Phase 1 (see graphic below). While the purpose of Phase 1 studies is primarily to learn about safety and pharmacokinetics (PK) and pharmacodynamics (PD), i.e., where and how drug is taken up in the body, MATRIX will also be looking to better understand the acceptability of products by incorporating socio-behavioral research into all of its Phase 1 studies and by conducting placebo studies of prototype products with no active drug.

MATRIX: All about early research and development



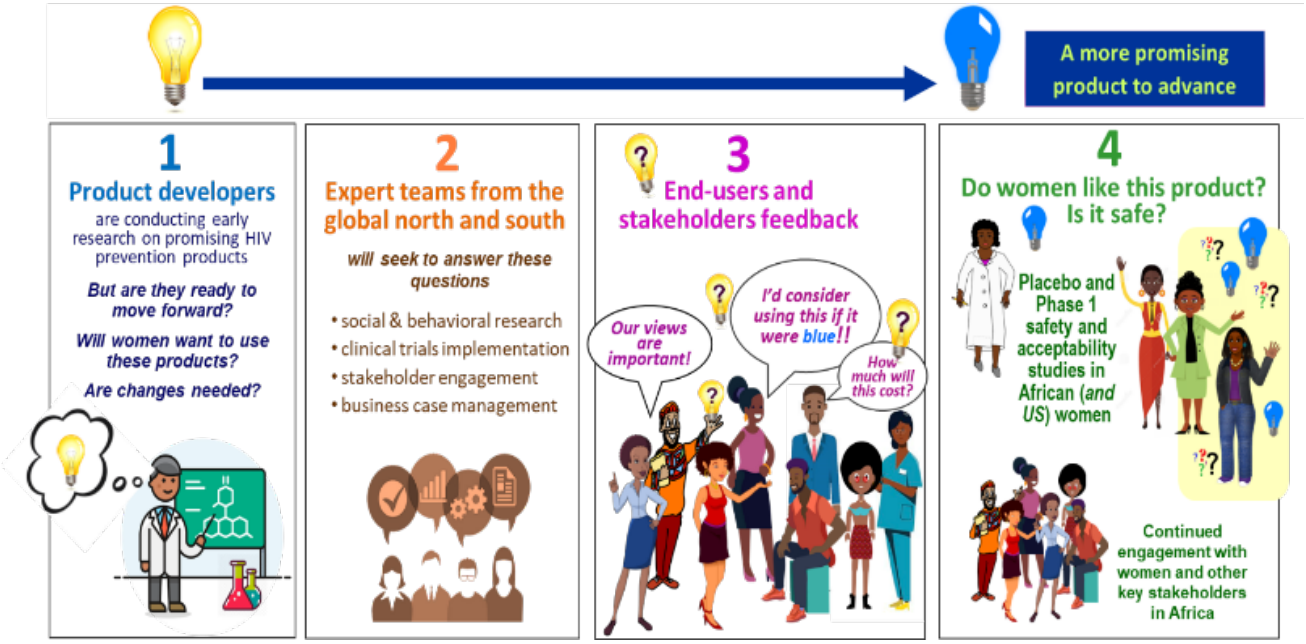
Moreover, MATRIX will be breaking new ground by conducting early phase (Phase 1), including first-in-human, clinical trials and placebo studies in sub-Saharan Africa in parallel with those in the U.S. According to information available on ClinicalTrials.gov, of some 1,611 HIV-related first-in-human and Phase 1 trials conducted globally, less than 10 percent were conducted in sub-Saharan Africa[4]. Most HIV prevention studies that have taken place in Africa have been later phase studies (Phase 2 or 3) and were conducted only after Phase 1 safety studies among women (at low risk of HIV) in the U.S. or Europe had indicated it would be safe to do so. MATRIX intends to conduct these trials in Africa to gain important insight into the safety and acceptability of new products in the populations of women they are primarily intended for, and to do so much earlier in the process, so that a more promising product can advance to Phase 2 (and possibly Phase 3) evaluation.

Research and development of HIV prevention products is a long and complex process that can take many years with relatively few drugs or products succeeding. Of some 5,000-10,000 compounds considered for investigation, only 50, at most, typically make it to Phase 1 trials, and of these, perhaps only one will progress through Phase 2 and Phase 3 trials and eventually receive regulatory approval.

MATRIX has also adopted a unique approach that aims to improve the odds of success for the products in its portfolio that considers other metrics in addition to findings of animal and laboratory studies that suggest the product will be safe and effective. It must also be a product that end-users indicate they would use. As such, seeking the perspectives of potential end users and other stakeholders, including their views on preferred product characteristics, is an integral part of the process so that this feedback can inform decisions about a product's

[4] https://ClinicalTrials.gov Data accessed 7 September 2022

design. Other considerations for ensuring that only the most promising products advance to early phase clinical trials include whether there is potential for it to be manufactured and distributed locally and at low cost, whether it is likely to be easy to deliver with minimal burden on healthcare systems and whether it would align with the priorities of Ministries of Health and national HIV prevention programs.



Considering the views of end-users and stakeholders from the start

Once a product developer has demonstrated the safety and potential effectiveness of a product in laboratory and animal studies, the next step is to conduct a first-in-human Phase 1 clinical trial in a small number of healthy participants, with additional Phase 1 trials likely to follow. Phase 1 studies are conducted primarily to evaluate the safety of the product and to see how and where the drug is taken up in the body. Phase 1 studies will sometimes look at acceptability as well – Do participants find the product easy to use? Are they experiencing side effects? Would they consider using the product if it were ever to become available? Phase 1 studies of HIV prevention products, particularly those involving women, are more often than not conducted in the U.S. or Europe. This means the data collected will be specific to these populations of women – not the population of women the product is intended to be used by.

MATRIX intends to conduct Phase 1 studies in sub-Saharan Africa, as well as in the U.S. Moreover, before even proceeding with a clinical trial, researchers will seek the feedback of potential end-users and stakeholders to ensure the right product – the one most likely to be used and also practical and feasible to introduce – is what moves forward. In the simplified scenario described above, feedback received from end-users and stakeholders indicates that the product in question wouldn't be acceptable unless it were the color blue. The product developer makes the necessary modifications, and this is the product that then proceeds into Phase 1 trials.

How MATRIX is organized

MATRIX is being implemented by Magee-Womens Research Institute (MWRI), in close collaboration with 19 partner organizations from North America and Africa. Through its North-South partnerships, MATRIX aims to recognize and strengthen the research and development capacity of African investigators to conduct early phase and first-in-human trials, and to facilitate full and sustainable ownership of this work into the future. Leading the project are Sharon Hillier, Ph.D., of MWRI and the University of Pittsburgh, USA, who serves as director, and Thesla Palanee-Phillips, Ph.D., from the Wits Reproductive Health and HIV Institute (Wits RHI) and University

of the Witwatersrand, South Africa, who is deputy director. Its 19 partners include four product developers – all based in the U.S.: CONRAD, a nonprofit organization affiliated with the Eastern Virginia Medical School; Oak Crest Institute for Science; Population Council; and the University of Pittsburgh.

Studies will be conducted in both the U.S. and at MATRIX 's five African partner sites: in Kenya, at the Kenya Medical Research Institute (KEMRI); in South Africa, at the Aurum Institute, Centre for the AIDS Programme of Research in South Africa (CAPRISA) and Wits RHI; and in Zimbabwe, at the Harare Health and Research Consortium (HHRC).

MATRIX's structure consists of five activity hubs:

- **Technology Accelerator** manages the development process of the MATRIX product pipeline, and with the input of an independent Scientific Advisory Group, advises on a product's next steps, i.e., whether it can proceed to a placebo study or Phase 1 clinical study, whether additional animal and laboratory studies and/or product design modifications are needed; or whether to stop its development. The Technology Accelerator also provides support to other research and development endeavors by providing seed funding for projects investigating novel approaches, including of projects led by African investigators.
- **Clinical Trials** matches product developers with trial sites in the U.S. and Africa and provides input on trial design.
- **Design to Delivery (D2D)** includes three components, one that conducts end-user research to understand women's preferences for different MATRIX products and product attributes; a second that designs and implements behavioral studies and socio-behavioral research within clinical trials, and the third which focuses on engaging with and seeking feedback of stakeholders regarding MATRIX's products, proposed studies and its overall research process.
- **Business, Market Dynamics and Commercialization (BACH)** conducts business case and market analysis as well as seeks linkages with possible investors.
- **Capacity Strengthening, Engagement and Mentorship (CaSE)** matches African investigators with mentorship and fellowship opportunities, with an emphasis on early research and development.

MATRIX Stakeholder Consultations in Africa

In October and November 2022, MATRIX partners convened its first in-country consultations in South Africa, Zimbabwe and Kenya. These meetings served to introduce the new project to stakeholders and seek their feedback on the HIV prevention products being developed under MATRIX. The meetings were conducted with the following objectives in mind:

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 sub-Saharan Africa and discuss ways to mitigate potential community concerns.
3. Seek stakeholders' feedback on each of the products in the MATRIX pipeline.
4. Establish a foundation for ongoing, bi-directional engagement with stakeholders through the life of the project and the product development lifecycle.

Consultations were conducted on 5-6 October in Johannesburg, South Africa; 18-19 October in Harare, Zimbabwe; and 8-9 November in Nairobi, Kenya. A wide range of stakeholders from the HIV prevention and maternal and reproductive health arenas attended the meetings, including ministries of health officials and other policymakers, regulators, ethicists, advocates, civil society, providers, implementers, other researchers, community representatives, former study participants, adolescent girls and young women and potential end-users, among others. Pre-meeting workshops for advocates, adolescent girls and young women and community representatives took place the day before each of the consultations. The South Africa consultation was attended by 30 external stakeholders, while attendance in Zimbabwe and Kenya was 51 and 57, respectively. Also in attendance were MATRIX in-country partners and representatives of USAID.

Each of the three meetings was guided by an agenda that was designed to be highly interactive, included the voices of young women and potential end-users and allowed time and space for rich discussion by all stakeholders. Presentations that served to set the stage provided an overview of the current HIV prevention landscape, described the MATRIX project and its mission and approach to research and development and focused on understanding what the process of product development entails, in particular early phase clinical trials, and sensitizing stakeholders to the realities – that very few products make it all the way through to regulatory approval. These presentations were followed by interactive sessions using polling software to gauge stakeholders' views on whether additional HIV prevention options (besides oral PrEP, dapivirine ring and CAB-LA) are needed, including on-demand products and MPTs designed to protect against HIV as well as other STIs and/or unplanned pregnancy.

Why stakeholder consultations?

"We want to integrate all of the feedback that we get at this meeting – as well as future meetings, small group meetings, one-on-one chats – into the research and development process."

– Thesla Palanee-Phillips, Wits Reproductive Health, and HIV Institute (Wits RHI), South Africa

"At the end of the day, we want a toolbox with multiple options so we can offer choice to women, like in family planning."

– Leila Mansoor, Centre for AIDS Research Programme in Africa (CAPRISA), South Africa

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

– Nyaradzo Mgodi, Harare Health Research Consortium (HHRC), Zimbabwe

"MATRIX is all about improving the chances of success…a new way to do things by involving communities early… At the end of the day, we want products that are affordable, not just beautiful products sitting on shelves… we want products that are safe, easy to distribute, easy to use, comfortable to use…"

– Nelly Mugo, Kenya Medica Research Institute (KEMRI), Kenya

"With MATRIX, we are putting the horse before the cart."

– Kenneth Ngure, Jomo Kenyatta University of Agriculture and Technology (JKUAT), Kenya

Stakeholders were also asked to provide their views on the specific products being developed under MATRIX and on the notion of early-phase clinical trials, including first-in-human studies, being conducted in sub-Saharan Africa. Six products in the MATRIX pipeline were discussed following pre-recorded video presentations provided by each of the product developers, with more in-depth discussion focused on the three products closest to being evaluated in women:

- The TAF/EVG fast-dissolving vaginal insert, which will be evaluated in a Phase 1 study – the first study of the product involving African women
- The one-month dapivirine vaginal film, which before being evaluated in a first-in-human trial, researchers will assess the safety and acceptability of two prototype placebo films in the first study of a film that is intended to take one month to dissolve
- The non-ARV, non-hormonal contraceptive MPT vaginal ring, which as with the dapivirine film, a study of placebo prototypes would be conducted first



Mariah Onyango, an advocate with the Network for Adolescent and Women Inclusion in Reproductive Health and Rights, Kenya

Overview: Stakeholders' views on the need for new HIV prevention options for women and the products being developed under MATRIX

MATRIX is seeking to increase the number of methods and products for women to protect themselves against HIV, but do stakeholders agree? The three in-country consultations sought to hear stakeholders' views about whether they see a need for new biomedical prevention products, in addition to oral PrEP, the dapivirine vaginal ring and CAB-LA, including products that are on-demand (used at or around the time of sex); would protect against more than HIV (multipurpose prevention technologies); or would protect against HIV acquired through anal sex. More specifically, stakeholders were asked to share their views of the products in the MATRIX pipeline.



Jacintah Nyokabi, Senior Field Officer, Kenya Medical Research Institute Centre for Clinical Research - Partners in Health and Research Development, uses a hand-held device to register her views

Meeting organizers made use of audience polling software to record meeting participants' anonymous responses to multiple-choice questions. Point Solutions (Echo360.com) was used in South Africa and Kenya, while Mentimeter (Mentimeter.com), an online audience poll system, was used in Zimbabwe due to technical difficulties with Point Solutions software. Facilitated discussion took place after the results were displayed, although discussion was not limited to these specific sessions. Of note, the views of some stakeholders changed or evolved over the course of the meetings as more information was presented and they came to better understand the issues.

Across all meetings, the majority of stakeholders agreed on the need for additional HIV prevention methods. Of the products being developed under MATRIX, the non-ARV, non-hormonal contraceptive MPT vaginal ring excited stakeholders the most, with the TAF/EVG fast-dissolving insert and the two cabotegravir products being ranked either second or third. While there was overall support for on-demand products, stakeholders felt strongly that the duration of protection they provide be at least 24-48 hours, and as such, felt that the Griffithsin fast-dissolving insert needed to offer more than four hours of protection. Stakeholders were, for the most part, enthusiastic about the monthly dapivirine vaginal film, although there were also questions about how well women would take to using it. After seeing and touching prototype placebo films that meeting organizers passed around, stakeholders in South Africa and Kenya were far more skeptical about the film being a viable option for HIV prevention. The dapivirine film was the only product put to such a test, as prototypes of the other products were not available for circulation during these in-person consultations.

While stakeholders in Kenya had comparatively more concerns about women's use of and interest in vaginal products, overall, stakeholders across all three countries supported and were impressed with the range of products being explored under MATRIX because, after all, the needs and preferences of women are not the same, and so different options are needed. Although no one disagreed on the importance of having choice, in South Africa this was also a sensitive topic for advocates frustrated with country-level decisions not to give women access to the dapivirine vaginal ring, a woman-controlled, non-systemic method already found to be safe and effective: How could they advocate for early-stage products that, even if successful, would be years away from approval, without first ensuring women had what tools were available today?

In the several pages that follow are the responses to polling questions asked at each of the consultations as well as relevant quotes reflecting some of the sentiments and views expressed by stakeholders during the course of these meetings.

Stakeholders' views on the need for new HIV prevention methods

Are other HIV prevention options needed?

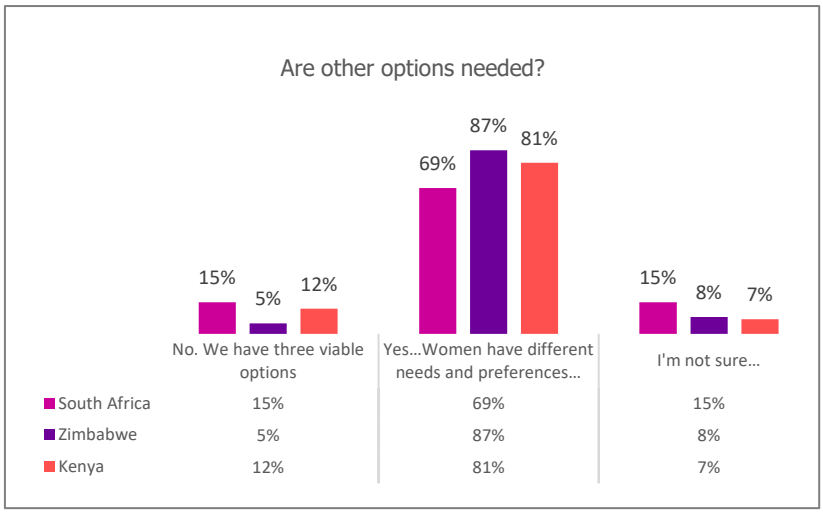
The first question asked of stakeholders was whether additional HIV prevention options were needed besides oral PrEP, the dapivirine vaginal ring and CAB-LA. Across all three countries, the majority of meeting participants agreed that new options are needed, because women have different needs and preferences. At the same time, and in South Africa, particularly, it was felt that more should be done to ensure national programs do their part to make newly approved methods, such as the dapivirine ring and CAB-LA, available to the populations who truly need much more than oral PrEP. Of note, early into the Zimbabwe meeting, Liberty Chirinda, the Chief Regulatory Officer for the Medicines Control Authority of Zimbabwe (MCAZ), announced the agency had approved CAB-LA, the first African country to do so.

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?



"For many years women have been robbed of the power to make choices… We want to see young women able to access products they have power and choice over… having many options that are discreet, that are comfortable, that women can control, that are long-acting or short-term depending on what a woman would want – and most importantly that are available – will go a long way in ensuring that we reduce HIV prevalence infection in our countries."

- Jerop Limo, Executive Director, Ambassador For Youth and Adolescents Reproductive Health Programme, Kenya

"We are the next generation that will help end AIDS and we need all the tools we can get. Make the ring a reality and then continue searching for new products."

- Chantel Maganye, former REACH (MTN-034) study participant, MOSAIC NextGen Squad member, South Africa



"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."

- Havana Mtetwa, Youth Advocate and MOSAIC NextGen Squad member, Zimbabwe

"When I deal with adolescents and other young people at the facility, they complain about oral PrEP, about the pill burden, about having to take the pill every day."

- Leonidah Ayuma, Youth Advisory Champions for Health, Kenya

"Can we have more products that people can get over the counter and not have to go to the facility?"

- Hasina Subedar, Senior Technical Advisor, National Department of Health, South Africa

"One new [HIV] infection is one too many, we have to do whatever we can to avert this."

- Takunda Sola, HIV Prevention and Key Populations Clinical Officer, Ministry of Health and Child Care, Zimbabwe

What are views on the need for on-demand products?

As shown in the following chart, the majority of stakeholders felt there was a need for on-demand products. Across all meetings, 83 percent of the responses reflected a view that such products would appeal to women having occasional sex or those simply wanting to use a non-systemic approach. Stakeholders also were cognizant that on-demand products may not work for everyone, and for various reasons, including the fact that women cannot always anticipate exactly when they will be having sex. As such, the majority preferred a product that would offer protection for at least 24 hours, with nearly two-thirds in Zimbabwe preferring at least 48 hours of protection. Additional feedback regarding on-demand products was provided during the sessions on the TAF/EVG fast-dissolving insert and Griffithsin fast-dissolving insert and are included in the next section, Stakeholders' Views and Feedback Regarding the MATRIX Pipeline of Products.

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Two of the products in the MATRIX pipeline are of the kind sometimes referred to as "on-demand" because they are to be used at or around the time of sex. Both are fast-dissolving inserts that when placed inside the vagina release the active agent as it slowly dissolves. Women would insert these themselves. What are your views regarding on-demand products for HIV prevention?

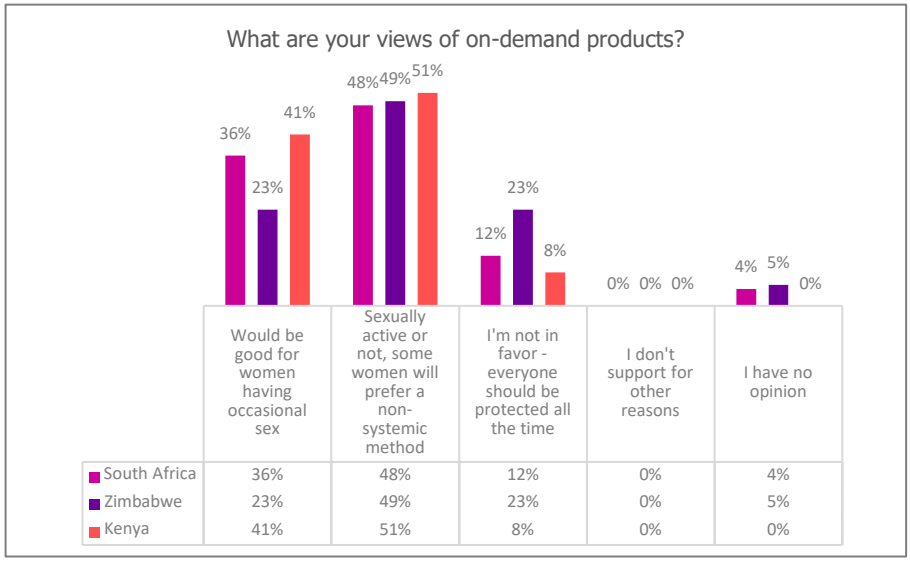
A. These kinds of products would be good for women who are only having sex occasionally and are likely to be preferred over a method needing to be used daily or that is long-acting.

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



"I believe everyone needs what works for them, and this will be good for those that don't want a continuous method."

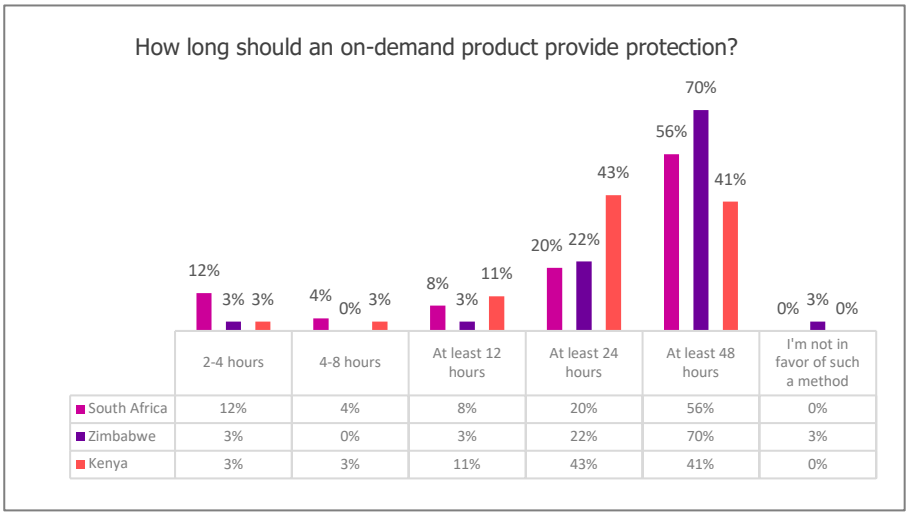
- Stakeholder, Kenya

"… some women will only need to use it when they know they'll have sex."

- Stakeholder, Kenya

"Sometimes sex is unpredictable, spontaneous, so on-demand products may not work."

- Mkhokheli Ngwenya, National Professional Officer, WHO, Zimbabwe



"This means that a lot of thinking that has to go on about whether or not you're having sex and whether you should put it in… sometimes sex is random, unplanned, that also happens. So, it's a bit of a challenge with the on-demand options when you don't really know whether or not you'll have sex."

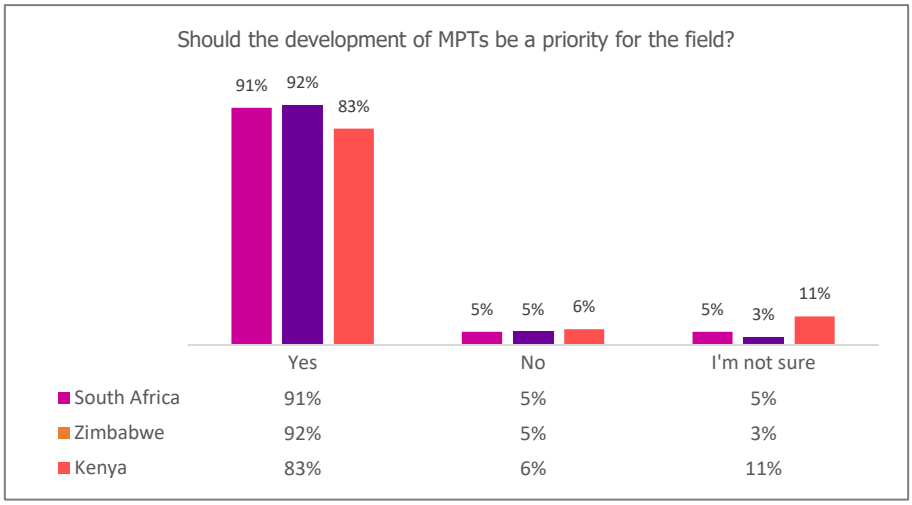
- Constancia Mavodza, Research Fellow, The Health Research Unit Zimbabwe (THRU ZIM), Zimbabwe

Should the development of multipurpose prevention methods be a priority?

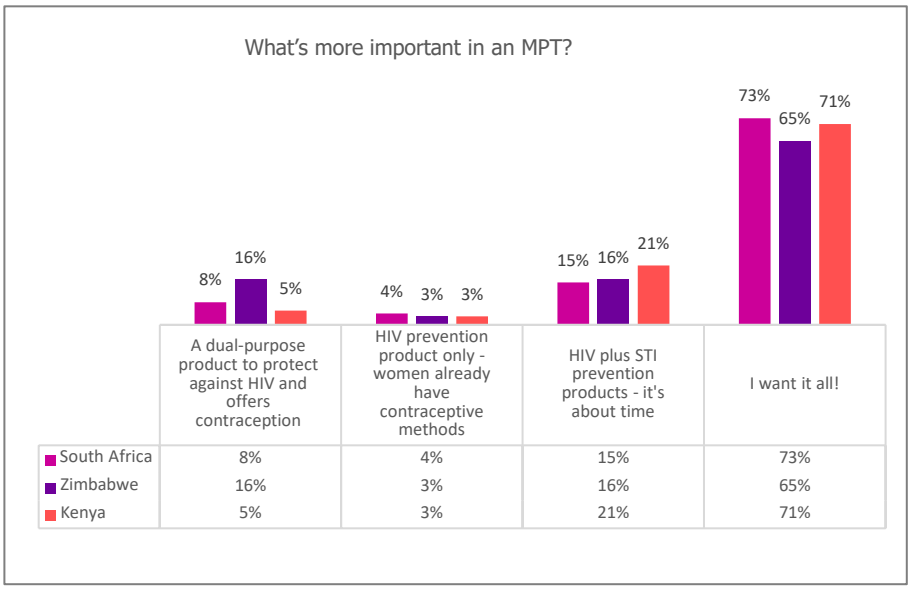
Stakeholders believed that the development of multipurpose prevention products (MPTs) was extremely important, with 89 percent across the three meetings saying MPTs should be a priority, and if given a choice, preferring products that did it all – provided protection against HIV, HSV, HPV and unplanned pregnancy. At the same time, there needed to be careful thinking and planning regarding their delivery.

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 unplanned pregnancy – products often referred to as an MPT, short for multipurpose prevention technology.

What is your opinion about MPTs – should their development be a priority for the HIV prevention field?



> ***"These days we say in Kiswahili, 'mambo ni mengi, muda ni mchache' (too much to do, too little time). I want a one-stop shop that meets all my needs all under one roof."***
>
> - Pamela Makokha, Meditrust Healthcare, Kenya



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

- Tendai Mbengeranwa, Key Populations Coordinator, National AIDS Council, Zimbabwe

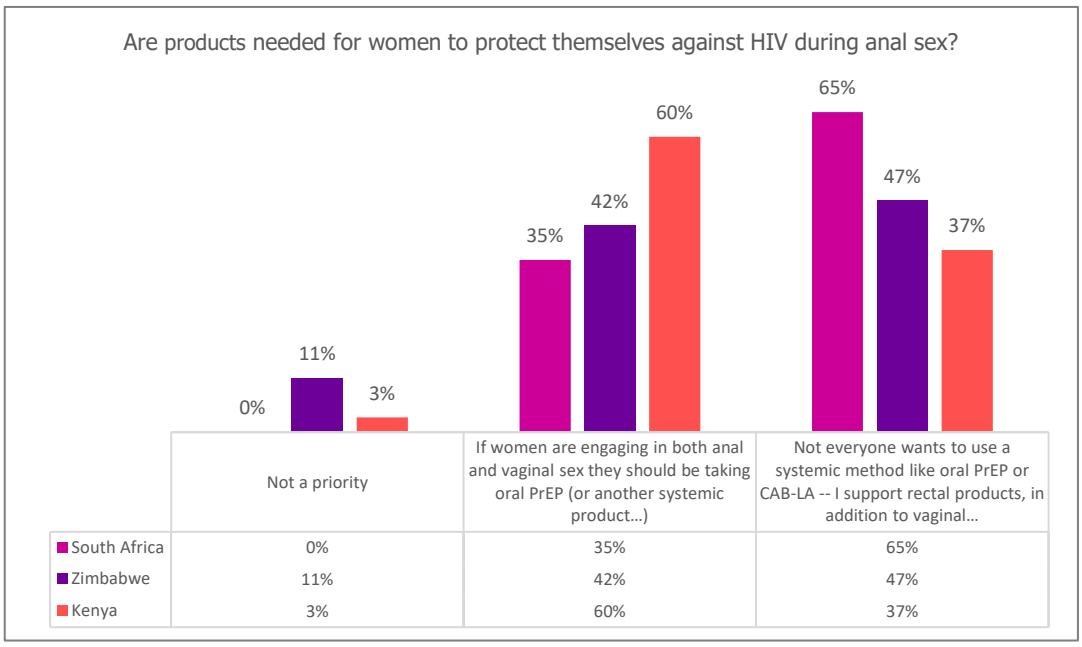
"These products are really exciting because combination prevention is needed. Trying to give someone one product for HIV, another for HPV, it's a lot."

- Primrose Matambanadzo, Centre for Sexual Health and HIV AIDS Research (CeSHHAR), Zimbabwe

"… [in] combining contraceptives with ARV, think about how [the product] will be delivered, who can prescribe it, where to obtain it, also whether it can be self-administered, because protocol or guidelines for delivering ARVs are much more rigorous than for family planning."

- Hasina Subedar, Senior Technical Advisor, National Department of Health, South Africa

What about products for women engaging in anal sex?

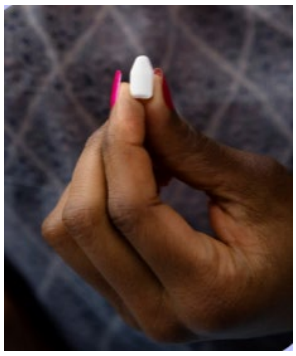


"It's important to consider this, as preference for anal sex with women increases, especially with commercial sex workers."

- Munyaradzi Chimwara, Advocacy Core Team (ACT), Zimbabwe

Stakeholders' views and feedback regarding the MATRIX pipeline of products

TAF/EVG fast-dissolving insert and the MATRIX-001 study



About the product

The TAF/EVG fast-dissolving vaginal insert is one of two on-demand products in the MATRIX portfolio. The product, which is being developed by CONRAD/Eastern Virginia Medical School, contains two anti-HIV drugs – tenofovir alafenamide (TAF), which also acts against HSV (herpes), and elvitegravir (EVG). Animal and laboratory studies suggest it would provide protection for up to three days after being inserted (women would insert it themselves) and could be used before or after sex (as either PrEP or PEP) and as either a vaginal or rectal product.

The MATRIX-001 Phase 1 study will evaluate the safety and acceptability of the insert used vaginally as well as where and how the drugs are taken up in the body. In addition, laboratory tests of tissue samples will be conducted to assess its potential activity against HIV and HSV. MATRIX-001 will be the fourth study related to the TAF/EVG insert. Studies relevant to its vaginal use include a study of the safety and acceptability of a placebo insert (with no active drug) among 32 women in the U.S. and the safety and acceptability of the active product with single use as a vaginal insert among 16 women in the U.S. Researchers need to know about the safety of the TAF/EVG insert with more frequent vaginal use (not just one time) and to understand its safety and acceptability in African women, not just women in the U.S. The MATRIX-001 study, which will enroll 60 women at three sites in the U.S., Kenya and South Africa, is the first to evaluate the insert in African women. Study results will determine whether the TAF/EVG insert should proceed to Phase 2 studies that would evaluate its safety and acceptability when used as designed – at or around the time of sex, and vaginally or rectally.

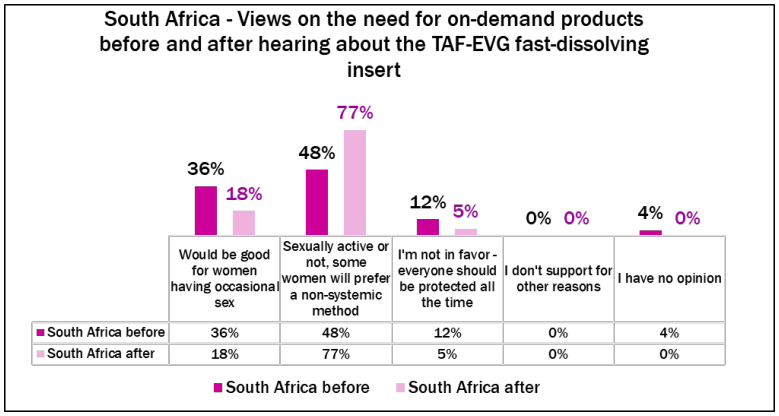
Stakeholders' views

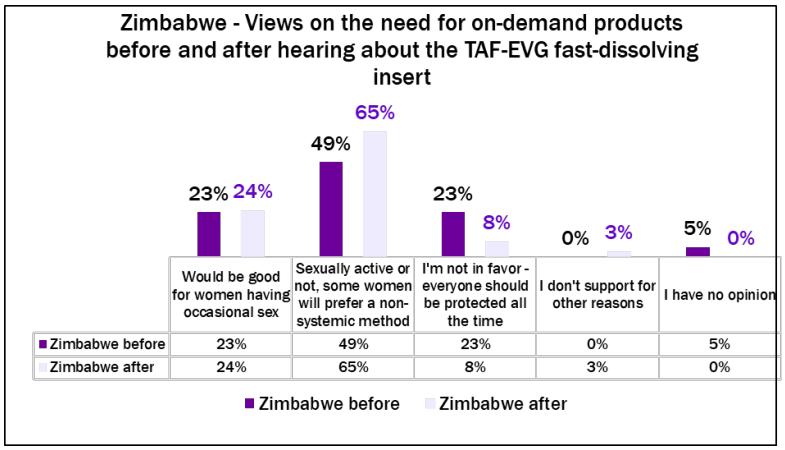
After hearing about the TAF/EVG fast-dissolving insert and MATRIX-001 study, stakeholders were polled a second time about their views of on-demand HIV prevention products. In each of the meetings, stakeholders had earlier indicated their support for these kinds of methods, with responses indicating they would be good for women engaging in occasional sex or appeal to women wanting a non-systemic method, regardless of their sexual activity. In total, this accounted for 83 of stakeholders supporting the development of on-demand products.

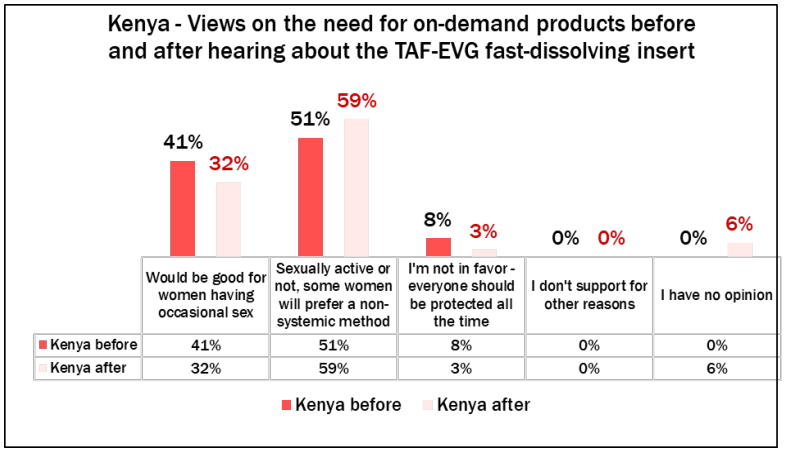
Asked the same question again, the level of support increased to 92 percent. The greatest increases were seen among South African and Zimbabwean stakeholders. In South Africa, a total of 84 percent of stakeholders indicated their support for on-demand products when first asked – either because these products would be good for women having occasional sex (36 percent) or would appeal to women wanting a non-systemic product, regardless of sexual activity (48 percent). After hearing about the TAF/EVG insert, their level of support increased to 95 percent, with 77 percent voting in favor of the product as an option for women preferring to use a non-systemic method. In Zimbabwe, the level of support was initially 72 percent and jumped to 89 percent. Kenyan stakeholders' support had been high and remained high, at 92 and 91 percent. Across all three countries, the fact that on-demand products were non-systemic appeared to be the most appealing feature.

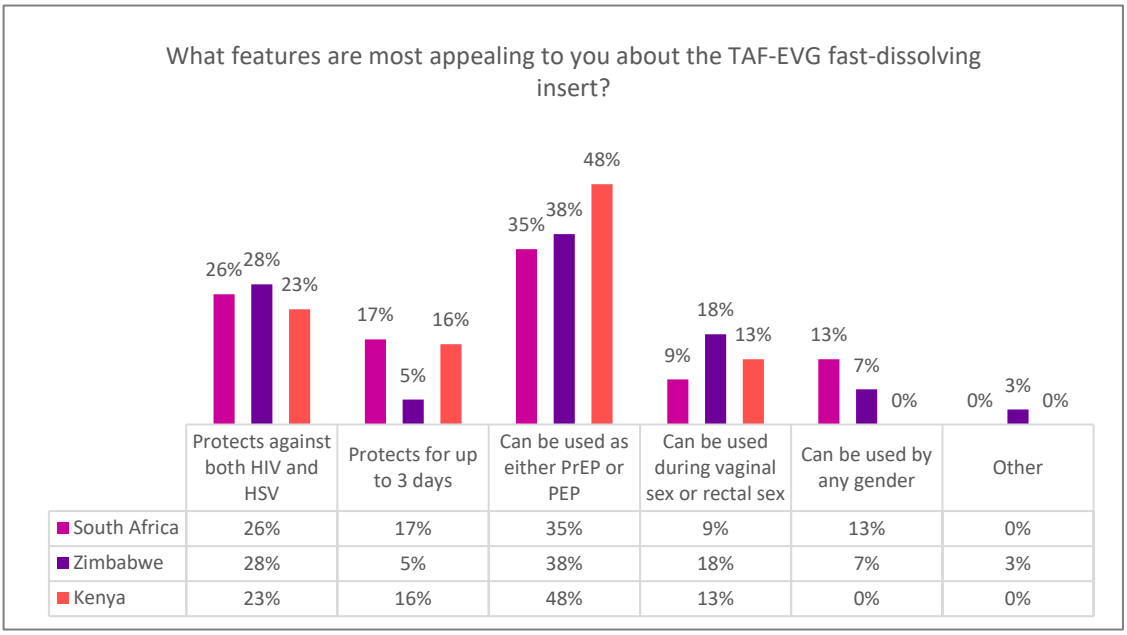
Asked what was the most appealing or most important feature of the TAF/EVG insert, 40 percent of stakeholders across the three meetings liked that it could be used as either PrEP or PEP and 26 percent said what was most appealing was that it would protect against both HIV and HSV.

Some expressed concerns about the method of insertion, that women were expected to insert the product using only their fingers and suggested that an applicator might make this easier. The researchers explained that the MATRIX-001 study would assess any difficulties or challenges women may have with insertion. In all three countries, meeting participants also wanted to know whether menstruation would impact the effectiveness of the insert. Again, the research team explained that this was not yet known, and that MATRIX-001 was not designed to answer this question. Women in the study would be using either the TAF-EVG insert or a placebo with no active drug over two weeks when women are not having their periods. Women would also be required to abstain from sex during this time so that the study can assess the safety and understand how the drug gets distributed under more controlled conditions, i.e., without menstruation or penile-vaginal sex being variables. Provided MATRIX-001 finds no safety concerns, additional studies (Phase 2) designed to answer these kinds of questions would be conducted, and its effectiveness would be evaluated if and when the product were to advance to Phase III trials.









	Protects against both HIV and HSV	Protects for up to 3 days	Can be used as either PrEP or PEP	Can be used during vaginal sex or rectal sex	Can be used by any gender	Other
South Africa	26%	17%	35%	9%	13%	0%
Zimbabwe	28%	5%	38%	18%	7%	3%
Kenya	23%	16%	48%	13%	0%	0%

"If this product succeeds in the trials, I believe it's going to be a game changer."

- Ferdinand Adungo, Senior Research Scientist, Kenya Medical Research Institute, Kenya

"I like TAF/EVG because it is used for both PrEP and PEP. So that will eliminate a lot of inconveniences, when you have one product which can be used for both needs."

- Tinashe Mudzviti, Chief Pharmacist, Newlands Clinic, Zimbabwe

"On short-term products, we learnt during the COVID pandemic that clients using short-term family planning products are at a disadvantage - those clients [had] difficulties in accessing services. So, this would be a minus…"

- Tsitsidzaishe Musvosvi, Director, Service Delivery and Training, Zimbabwe National Family Planning Council (ZNFPC), Zimbabwe

One-month dapivirine vaginal film and MATRIX-002 study

About the product



The one-month dapivirine vaginal film is a discreet, woman-controlled method being developed by the University of Pittsburgh that researchers anticipate will be easy to manufacture and distribute at low cost. The idea is that once the film is placed inside the vagina, it would slowly begin to dissolve, and in doing so, release the ARV dapivirine. Drug would continue to get released until the film completely disappears – this means that all drug contained in the film would be distributed within the vagina and there would be nothing to discard or remove. Dapivirine has already been shown to be safe and effective as a vaginal ring, with the ring having been approved in several countries.

A daily quick-dissolve film and a 7-day film were found to be safe and acceptable in U.S. women, and the feasibility of a monthly vaginal film has been demonstrated in studies of nonhuman primates. Before conducting a first-in-human Phase 1 study of the monthly dapivirine film, researchers need to know that African women will

be comfortable with the idea of using a monthly film and are able to insert it. As such, plans are to first conduct a study to assess the acceptability of two different one-month placebo films as well as its safety and persistence (whether it remains in the vagina).

MATRIX-002 will enroll 60 women at five trial sites in the U.S., Kenya, South Africa and Zimbabwe. Women will be in the study for two months. During the first month of film use, they will be asked to abstain from sex so that researchers can establish a baseline for user acceptability. Results of MATRIX-001 – the first study of a film designed to dissolve over one month – will help inform the exact design of the active product to be tested in a Phase 1 study.

Stakeholders' views

The majority of participants in each country thought the monthly dapivirine vaginal film would be an important option for women who would prefer longer-term protection that is also non-systemic. Asked about the features that were most appealing about the film, the fact that it was non-systemic received the most votes at the Zimbabwe consultation, though other features were also deemed appealing by stakeholders at the three meetings. Notably, in South Africa, nearly one-third of stakeholders thought the concept of a vaginal film would be foreign to women and difficult to understand.

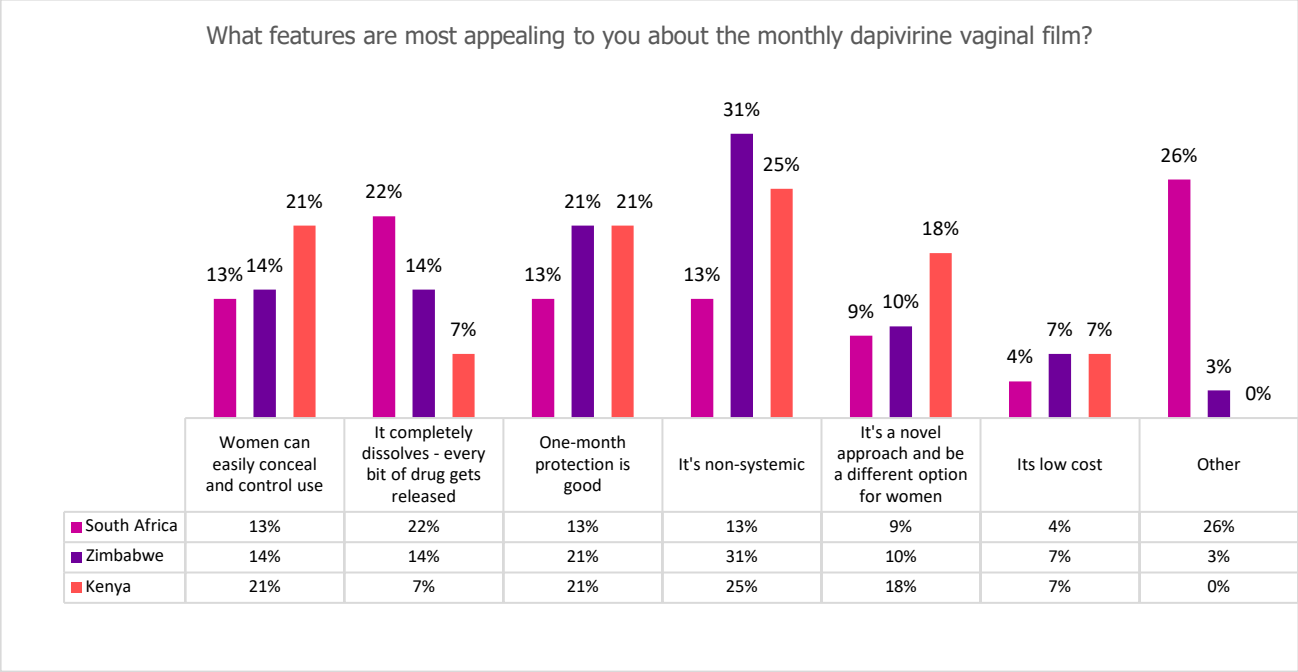


Wendy Adamba from Population Services Kenya examines two placebo vaginal films

At each of the consultations, prototype placebo films were passed around midway through the discussion for meeting participants to examine, touch and feel. When asked again about their views of the vaginal film as a method for HIV prevention, opinions of stakeholders in South Africa and Kenya shifted. Whereas before, 19 percent of Kenyan stakeholders liked that it was small and discreet, after seeing sample films, only 4 percent thought so. Similarly, views about the film being foreign to women jumped from 4 percent to 35 percent in Kenya and from 30 percent to 50 percent in South Africa, with views that it would be an important option for women wanting longer-term and non-systemic protection decreasing to 25 percent from 48 percent in Kenya and to 50 percent from 70 percent in South Africa.

Opinions in Zimbabwe, on the other hand, were basically unchanged, with 71 percent saying it was an important option in the first poll and 69 percent saying so after seeing and touching the sample films. One stakeholder had spoken earlier about her experience using a quick-dissolve placebo film as a participant in the QUATRO study, saying that she had no problems.

Across all three meetings, the **size and shape of the** film generated the most comments and questions, with several South African and Kenyan stakeholders doubting that women would be able to insert it, or want to, for that matter. The corners were seen as too sharp. In Kenya, stakeholders reported that many women don't like putting things in their vaginas. In both Zimbabwe and Kenya, there was concern that in areas with poor access to water women wouldn't be able to observe proper hygiene before using their fingers to insert the film. In all countries, stakeholders wondered whether the film would attach itself midway during insertion and whether it would be better to provide an applicator, with questions also in South Africa and Kenya about whether women with long nails would be able to insert the film (and whether their nails would puncture it). Regarding the MATRIX-002 study, stakeholders felt that requiring women to abstain from sex in the first month would present a challenge for recruitment. They also suggested that the study should involve male partners, whose support would be needed, but who would also be able to provide their perspectives of the film and what they experienced during sex, including oral sex. As a stakeholder in South Africa said, if it tastes like an ARV, that will be a turn-off.



	Women can easily conceal and control use	It completely dissolves - every bit of drug gets released	One-month protection is good	It's non-systemic	It's a novel approach and be a different option for women	Its low cost	Other
South Africa	13%	22%	13%	13%	9%	4%	26%
Zimbabwe	14%	14%	21%	31%	10%	7%	3%
Kenya	21%	7%	21%	25%	18%	7%	0%

"I won't keep forgetting to take it, it will save me from anxiety that I may forget."

- Josephine Achieng, Bar Hostess Empowerment & Support Programme, Kenya

"I think it is good empowerment to women because you will be able to administer at your own time and you don't need to go to the clinic, no need for healthcare."

- Adelaide Nyamwanza, Community Advisory Board member, University of Zimbabwe, Clinical Trials Research Centre (UZ-CTRC), Zimbabwe

" … I don't like inserting anything into my vagina … and what if it doesn't dissolve?"

- Gcobisa Madlolo, young woman advocate, South Africa



Gcobisa Madlolo

"[The film] was easy [to insert]. So, once you put it in there, then if you remove the finger it will stick in there…With the film actually my partner couldn't feel if there is something in there."

- Nyarai Moyo, former QUATRO study participant, Zimbabwe



Former QUATRO study participant Nyarai Moyo (R) shares a laugh with Chido Kaseke, a nurse at Wilkins Hospital – as he opens the package containing a placebo vaginal film during the consultation in Zimbabwe.

"How can we expect to put something square in a round hole?"

- Yvette Raphael, Executive Director, Advocates for the Prevention of HIV in Africa (APHA), South Africa

" Inserting, looks like you may literally have to push it inside, like pushing a tampon …. But this is a paper, it means you have to push it in further with the finger, or it may get stuck on the wall".

- Jerop Limo, Executive Director, Ambassador For Youth and Adolescents Reproductive Health Programme, Kenya

"Can they add lubricant to the film, to make it easy to insert? It feels rough."

- Shantele Mbuzi, former REACH (MTN-034) study participant, Zimbabwe

"In some women [with dry vaginas] it might just sit there like a kite."

- Mopo Radepe, Technical Officer, HIV Prevention, WHO, South Africa

[After immersing the product in water] "it immediately becomes soft, it is not hard anymore, but I think many women would prefer something without sharp edges and not square."."

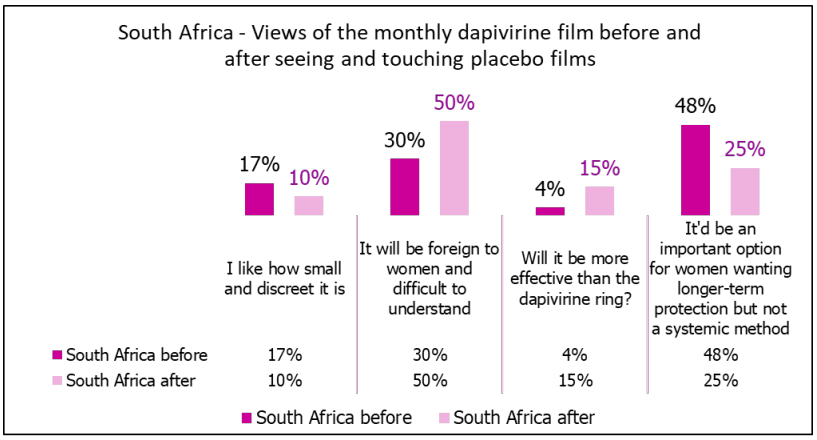
- Margaret Akinyi Atieno, AYP Liaison Officer, LVCT Health, MOSAIC NextGen Squad member, Kenya

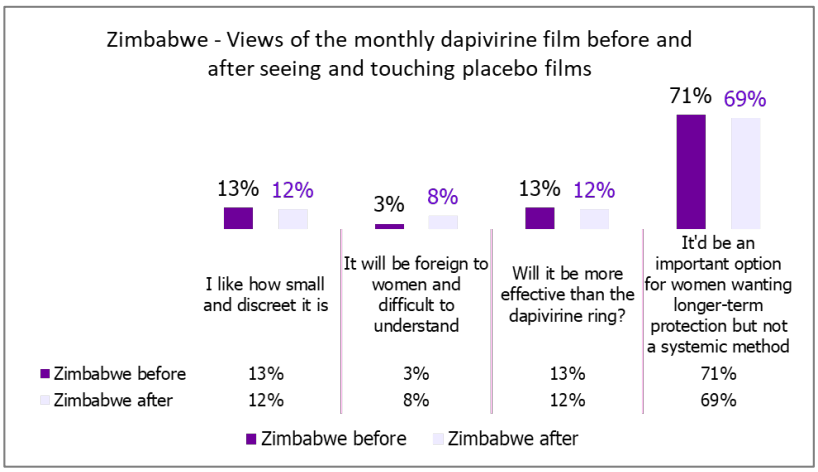
"I think it is a good product, it looks good to me, and it is something that can be used by many women."

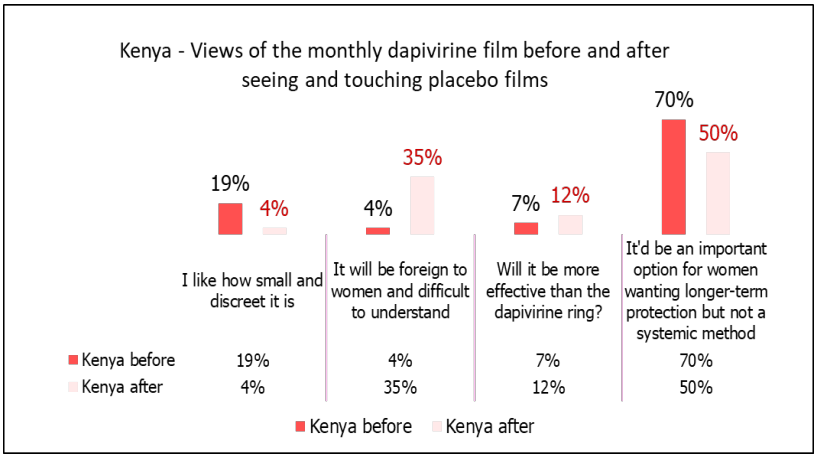
- Mavis Kambiro, Community Advisory Board member, UZ-CTRC, Zimbabwe

"I hear about the concerns around acceptability, but the idea is having a toolbox with many choices; you pick what you prefer …"

- Munyaradzi, Chimwara, Advocacy Core Team (ACT), Zimbabwe





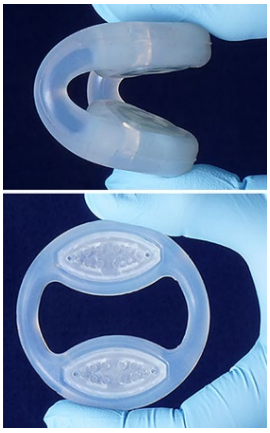


"On second thoughts I actually like it better, I can see myself using this, the corners we thought are sharp, can be folded in like this [demonstrates], so I think it would work."

- Marie Merci, MOSAIC NextGen Squad member, Kenya

Non-ARV, non-hormonal contraceptive multipurpose vaginal ring (LAMP-IVR)

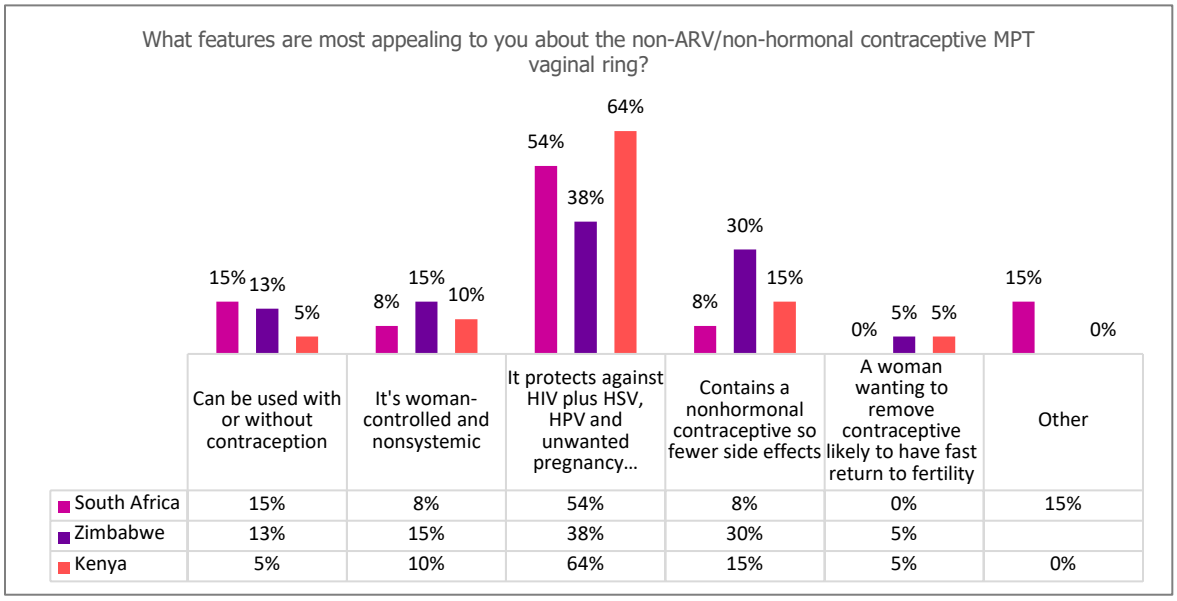
About the product



The Non-ARV, non-hormonal multipurpose vaginal ring (also referred to as the LAMP-IVR, short for Luminally Active Multipurpose Intravaginal Ring) is being developed by the Oak Crest Institute of Science as a method that would not only protect against HIV, but also HSV and HPV, and if so desired by the user, also against unplanned pregnancy for one to three months. The antiviral agent is a small protein fragment (peptide) that blocks viruses like HIV (HSV and HPV) from attaching to, penetrating and infecting healthy cells in the body. Because it is not an ARV, researchers believe drug resistance would be less of a concern should someone acquire HIV while using the ring. The contraceptive drug inhibits the movement of sperm and its ability to penetrate and fertilize eggs, and because it is not hormonally based, side effects such as irregular periods are not anticipated. Both agents are released independently from separate compartments within the ring – and in fact, it's this unique design that would allow women to use the ring with or without contraception, depending on needs and circumstances.

Stakeholders' views

Across all consultations, the majority of stakeholders indicated the most appealing feature about the ring was that it was a multipurpose prevention method, and in Zimbabwe, the fact that it contained a non-hormonal contraceptive was also appreciated by nearly one third of the meeting's participants. Questions about the ring's active ingredients dominated the discussion period at each of the three meetings, with stakeholders wanting to understand what these were exactly, and, in particular, what was meant by a non-ARV. While it was explained that it contains a peptide that acts as an anti-viral, little else has been disclosed by the product developer at the present time. Despite explaining that the kind of side effects associated with ARVs would not likely be an issue, participants still wondered what the potential side effects of the non-ARV might be. Stakeholders felt there needed to be more transparency, especially given the intention to conduct clinical trials in Africa. Unlike the dapivirine vaginal film, there were no prototype rings available at the meetings for stakeholders to touch and feel. Even so, based on the video presentation, stakeholders thought the ring was too large and too thick.



	Can be used with or without contraception	It's woman-controlled and nonsystemic	It protects against HIV plus HSV, HPV and unwanted pregnancy...	Contains a nonhormonal contraceptive so fewer side effects	A woman wanting to remove contraceptive likely to have fast return to fertility	Other
South Africa	15%	8%	54%	8%	0%	15%
Zimbabwe	13%	15%	38%	30%	5%	
Kenya	5%	10%	64%	15%	5%	0%

"The idea of having a non-hormonal contraceptive is good so I don't have to deal with issues of weight gain, irregular menses -- this is a big plus for me."

- Betty Mulinge, Kenya Pharmaceutical Association, Kenya

"Non-ARVs, non-hormonals are very appealing because right now we seem to be focusing so much on ARV- and hormonal-based products and there aren't many alternatives, so these are exciting."

- Hasina Subedar, Senior Technical Advisor, National Department of Health, South Africa

"As a young person, I like it because it is convenient, and I don't have to go to the health facility all the time. Once it is put in, I don't have to think about it, I can use my time for other things."

- Sinentlantla Gogela, Ground Force/Advocates for the Prevention of HIV in Africa (APHA), South Africa

Having a non-ARV non-hormonal product "is game-changing, it is really exciting to hear about this… [But] is efficacy of that peptide as guaranteed as the efficacy of an ARV?... Because right now, if you ask me to take a peptide or an ARV, I'll take the ARV. [Calling it non-ARV based] may undermine confidence in it by the "common person who for the last 30 years has heard about ARVs and they've seen how effective they are in addressing the HIV virus."

- Nonhlanhla Zwangobani, HIV Prevention Manager, Clinton Health Access Initiative (CHAI), Zimbabwe

Griffithsin fast-dissolving insert

About the product

The Griffithsin fast-dissolving Insert, which is being developed by the Population Council, is the second on-demand product in the MATRIX portfolio. Its active ingredient is a non-ARV protein derived from red algae that acts against HIV, HSV and HPV and gets released from the insert as it dissolves. Clinical, animal and laboratory studies suggest the insert could provide protection for at least four hours after vaginal insertion. As a non-ARV, researchers believe that it would likely have fewer side effects, and because Griffithsin is not used for HIV treatment, there would be less concern for emergence of cross-resistance. It would be a discreet method, easy to use and portable, and is anticipated to be inexpensive, scalable and able to be manufactured in low- and middle-income countries.

Stakeholders' views



Participants liked that the product was designed to protect against HIV, HSV and HPV and that it represented another on-demand option. The fact that it is based on a naturally occurring compound was also seen to be a potential advantage over other synthetic and drug-based products. Stakeholders in South Africa, however, felt that researchers needed to be careful about how the product is described to avoid the perception that seaweed or algae harvested from the sea alone would be protective against HIV . While meeting participants in all three countries welcomed the idea of the insert as an on-demand product, they expressed concern that the duration of protection the product would offer (four hours) was too short, because sex can't always be planned and may take place in situations that are longer than four hours, and therefore, the insert should ideally provide protection for at least 48 hours. At the same time, a few stakeholders raised the possibility that there might be women willing to make a tradeoff for a natural product that could protect against HIV, HSV and HPV, even if that window of protection was short.

Meeting participants wanted to know how fast the insert dissolves after being inserted into the vagina. In addition, they sought clarification on how many inserts an individual could use in a 24-hour period – could the product be inserted consecutively every four hours to extend the duration of protection? How many inserts would be considered an overdose? There was also concern that if a woman had to insert the product every four hours, it would no longer be discreet because her partner would notice. In addition, this would increase the overall cost if women had to be buying multiple inserts.

"You pop it in, and someone delays to come for sex -- this time is too short."

- Sarah Mkhabela, Ground Force/Advocates for the Prevention of HIV in Africa (APHA), South Africa

"I'd like a prevention method that gives me the confidence that I'm protected. I feel like with only four hours I'd be feeling very anxious."

- Betty Mulinge, Kenya Pharmaceutical Association, Kenya

"Let's say I have gone out with my boyfriend and the protection [of the product] is only for four hours. It is difficult -- I'd have to go back home. It is not guaranteed that it'd work, so it doesn't work for me."

- Tendai Mbengeranwa, Key Populations Coordinator, National AIDS Council, Zimbabwe

"If the woman has to get up to insert a fresh product every four hours, it undermines discreet use, the man will discover. We need products that a woman can use discreetly without having to explain herself."

- Patrick Mdletshe, Head of Community Programs, Centre for the AIDS Programme of Research in South Africa (CAPRISA), South Africa

"The potential for easy access, available over the counter, is very exciting and may help in normalizing HIV prevention … the potential for local manufacturing is also exciting."

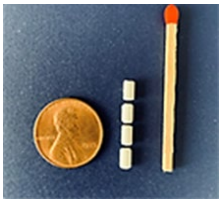
- Dominica Dhakwa, Chief of Party, Zimbabwe Health Interventions, Zimbabwe

Cabotegravir Dissolvable Pellet Implants and Cabotegravir Injectable Depot

About the products

Both products contain the ARV cabotegravir, which has been found to be highly effective against HIV when given as an intramuscular injection every two months, an approach known as CAB-LA. These newer formulations, which are being developed by CONRAD, would potentially provide longer protection – the dissolvable pellets for up to one year, and the injectable depot for four to six months. Unlike CAB-LA, they are to be administered just under the skin (subcutaneously), which would be less painful than intramuscular injection. They would also be easier and less costly to manufacture and deliver. Laboratory and animal studies conducted thus far suggest that drug persists in the body for a shorter period of time than with CAB-LA.





The exact dose of the pellet implants has not yet been determined, but it is estimated to be approximately fewer than 10 tiny pellets that would be inserted at the same time. Once inserted, the pellets would slowly dissolve over the course of a year, so there would be nothing to remove. If need be, the pellets could be safely removed within one to three months after insertion. With depot, cabotegravir is contained inside a small bubble-like gel that would slowly begin to dissolve after insertion, releasing the drug.

Stakeholders' views

Meeting participants gave both products high marks, but with caveats. Some of the stakeholders were concerned that healthcare workers would not have the proper skills to perform the procedures involved. For many of the young women, such concerns were based on their personal experiences with contraceptive implants. As for the injectable depot, stakeholders feared it might be confused with Depo-Provera, which in South Africa, would also have negative connotations, and, as such, wondered if it could have a different name. Young women also wanted

to know whether the pellet implants and depot would be visible or could be felt after insertion, which, if they did, would make them less discreet, and could potentially be cause for social or physical harm. A participant in South Africa cautioned that there had been cases of women with contraceptive implants being physically assaulted and their implants forcefully removed by perpetrators seeking the drug to get high, while in Kenya and Zimbabwe there were stories about women's partners, who upon discovering they had implants, would attempt to remove them by force. In South Africa, some of the young women worried that the pellet implants and injectable depot would be more difficult to insert and also be less effective in plus-size women.

Given concerns about CAB-LA's long PK "tail," stakeholders at each of the meetings wanted assurances that this would not be an issue for these newer products as well. With CAB-LA, a small amount of drug remains in the body for a prolonged period of time but at insufficient levels to protect against HIV, thereby posing a risk of development of drug resistance to ARVs in the same class, most notably dolutegravir. It was explained that because these products are delivered under the skin, rather than deep into muscle, drug is likely to remain in the body for shorter periods of time, which laboratory and animal studies conducted to date have shown, though research is still ongoing.

"I think young people would like it [CAB pellet implant] because it stays for a long time."

- Sarah Mkhabela, Ground Force/Advocates for the Prevention of HIV in Africa (APHA), South Africa

"To insert it seems an invasive procedure, then if after one or two months if I want them removed it will have to take the invasive procedure again."

- Leonidah Ayuma, Youth Advisory Champions for Health, Kenya

"I am concerned about provider competence to get them out, it may take time to remove, also with too many pellets means the provider has to make too many incisions … .During the time of Norplant, when we had five rods, it was not easy to remove them, sometimes we had to make three incisions to get them out."

- Pamela Makokha, Service Provider/Nursing Officer, Meditrust Healthcare Services, Kenya

"Consider the potential confusion with use of word depot in Cabotegravir Injectable Depot, as community is used to Depo Provera."

- Patrick Mdletshe, Head of Community Programs, CAPRISA, South Africa

"It [cabotegravir injectable depot] gives me time to continue with life without worrying about protection. Also because of the range, 6 months, and also because it is concealed. Some women need that freedom."

- Elizabeth Onyango, 2022 AVAC Fellow, COSWA, Kenya

"We would also like to find out how much tail is left with CAB products, and we expect this will come out in the clinical studies."

- Liberty Chirinda, Chief Regulatory Officer - Pharmacovigilance and Clinical Trials Division, Medicines Control Authority of Zimbabwe

Which products were stakeholders most excited about?

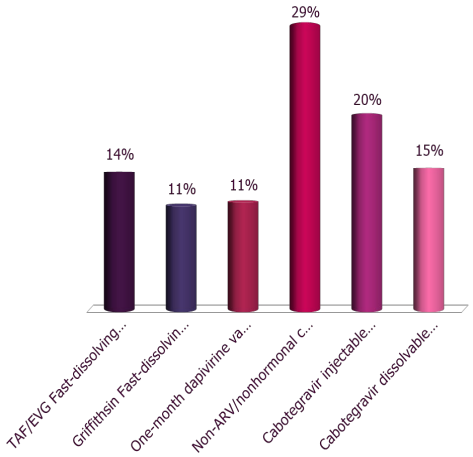
In the final session of the one and half-day meeting, participants were asked to cast their votes for the three products in the MATRIX product pipeline they were most excited about or felt were most needed, and to rank-order their responses The non-ARV non-hormonal contraceptive MPT vaginal ring (LAMP-IVR) ranked first across all three countries. Products ranked second and third, respectively, were: **South Africa** –cabotegravir injectable depot (#2) and cabotegravir dissolvable pellet implants (#3); **Zimbabwe** –TAF/EVG fast-dissolving insert (#2) and cabotegravir dissolvable pellet implants (#3); **Kenya** – TAF/EVG fast-dissolving insert (#2) and cabotegravir injectable depot (#3).

In reality, there were no clear winners or losers – stakeholders acknowledged the need for a range of products. Moreover, it would be up to women to decide what would work best for them based on individual circumstances, needs and preferences. What's important is that women have a choice in products, including those they can control themselves, are discreet and can be used without having to consult her partner, if need be; that are convenient to access and require minimal or no contact with healthcare workers; have few side effects and minimal impact on day-to-day activities and sex life; that are short-acting (on-demand) or long-acting, with options for non-systemic products; and multipurpose products that would protect against more than HIV. After the polling had closed at the South Africa meeting, one of the stakeholders admitted that she had not voted, because it didn't matter what she preferred when there would be other women who would prefer something else.

Which 3 products in the MATRIX product pipeline are you most excited about, or feel are most needed?

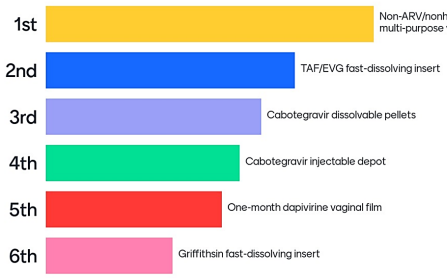
South Africa, using Point Solutions

1. Non-ARV/non-hormonal contraceptive MPT vaginal ring (LAMP-IVR)
2. Cabotegravir injectable depot
3. Cabotegravir dissolvable pellets
4. TAF/EVG Fast-dissolving insert
5. Griffithsin Fast-dissolving vaginal insert/ One-month dapivirine vaginal film



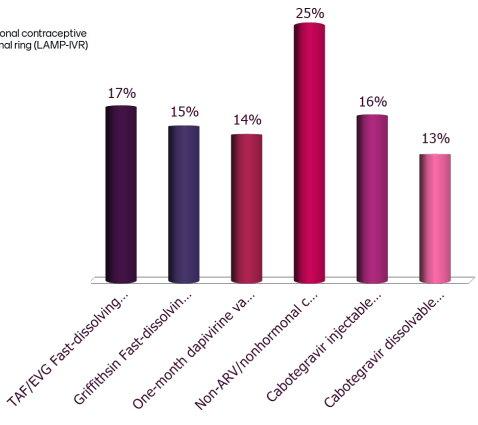
Zimbabwe, using Mentimeter

1. Non-ARV/non-hormonal contraceptive MPT vaginal ring (LAMP-IVR)
2. TAF/EVG Fast-dissolving insert
3. Cabotegravir dissolvable pellets
4. Cabotegravir injectable depot
5. One-month dapivirine vaginal film
6. Griffithsin Fast-dissolving vaginal insert



Kenya, using Point Solutions

1. Non-ARV/non-hormonal contraceptive MPT vaginal ring (LAMP-IVR)
2. TAF/EVG Fast-dissolving insert
3. Cabotegravir injectable depot
4. Griffithsin Fast-dissolving vaginal insert
5. One-month dapivirine vaginal film
6. Cabotegravir dissolvable pellets



"My favorite is the ring, because it offers what I have always wanted – one product to prevent HIV and pregnancy at the same time."

- Sarah Mkhabela, Ground Force/Advocates for the Prevention of HIV in Africa (APHA), South Africa

"We know from contraceptives and also ARVs that products with hormones can interfere with a woman's body, they disrupt menses and other metabolic processes, so the non-hormonal and non-ARV products would be best."

- John Mdluli, Head of Community Engagement, The Aurum Institute, South Africa

"I think all these products are allowing women to have power to make autonomous decisions about their sexual lives and to take care of themselves."

- Jerop Limo, Executive Director, Ambassador for Youth and Adolescents Reproductive Health Programme, Kenya

> ***"…it is important to appreciate that people have different tastes, different likes. One likes the film the other likes 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, you choose what you like."***
>
> - Munyaradzi, Chimwara, Advocacy Core Team (ACT), Zimbabwe

"In our cultures women don't have control, even when they know the husband is sleeping around, he has kids out there, they are not able to protect themselves. These products give women control."

- Gertrude Mungai, lifestyle and relationships advisor, Kenya

> ***"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."***
>
> - Talent Jumo, Founder and Director, Katswe Sistahood, Zimbabwe

"We have to …[understand] that is not about what's inside the method. … Women want products that allow personal choice that's based on their lifestyle, their need, their preferences, their context, their environment, they can say yes, I choose this, this is going to work for me."

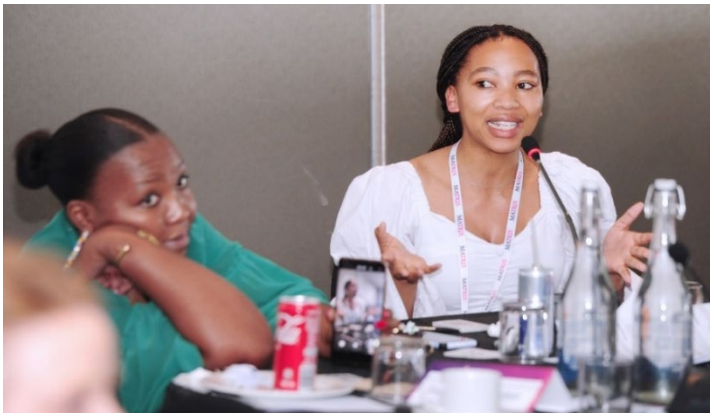
- Elmari Briedenhann, Technical Head, Programme Engagement, Wits Reproductive Health and HIV Institute, MOSAIC partner, South Africa

"If it is available at Clicks [local pharmacy], and we had the money to buy it, …[I'd] not have to go to the health center where the nurses ask me why I want to have sex."

- Sinentlantla Gogela, Ground Force/APHA, South Africa

"As an HIV advocate, I'm really excited that there's progress on MPTs that women can control, that there's a whole basket of choice for women. I'm proud that women will one day equitably access these products."

- Joyce Ng'ang'a, Policy Advisor, WACI Health; Coalition to Accelerate & Support Prevention Research (CASPR) Partner, Kenya



Sinentlantla Gogela (right) and Loyiso Saliso at the South Africa consultation. Both are with Advocates for the Prevention of HIV in Africa (APHA)

"A woman should not have to adapt her lifestyle to a product, the product should fit in her lifestyle."

- Blossom Makhubalo, Community Engagement Officer, Aurum Institute, South Africa

> ***"… we need a product that is not dependent on a healthcare provider, that could be more self-determined and self-acquired…"***
>
> - Hasina Subedar, Senior Technical Advisor, National Department of Health, South Africa

Should early phase clinical trials and placebo studies be conducted in sub-Saharan Africa?

Background

MATRIX activities are focused on the early development of products, which includes evaluating some products in humans for the first time. So far, first-in-human studies and other early phase (Phase 1) clinical trials of new HIV prevention products have mainly been conducted among women in the U.S. or Europe and only in later phase studies (Phase 2 or 3) have they been evaluated in Africa. MATRIX intends to break with the status quo by conducting Phase 1 trials, including placebo studies, in sub-Saharan Africa, in addition to and in parallel with studies in the U.S. In doing so, MATRIX hopes to gain important insights into the safety and acceptability of new products in the populations of women they are primarily intended for, and to do so much earlier in the process than has typically been the case in HIV prevention clinical research, so that a more promising product can advance to Phase 2 trials, and hopefully further. Conducting these studies in Africa would also enable skills and knowledge transfer between the Global North and South and enhance the capacity of African investigators and trial sites to implement such studies.

While Phase 1 studies are conducted primarily to understand the safety of a new drug or product and how and where the drug is distributed and taken up by the body, learning about its acceptability to the user is also important. MATRIX intends to incorporate socio-behavioral research into all its Phase 1 studies as well as conduct placebo studies – of prototype products with no active drug – to better understand what women want and will use.

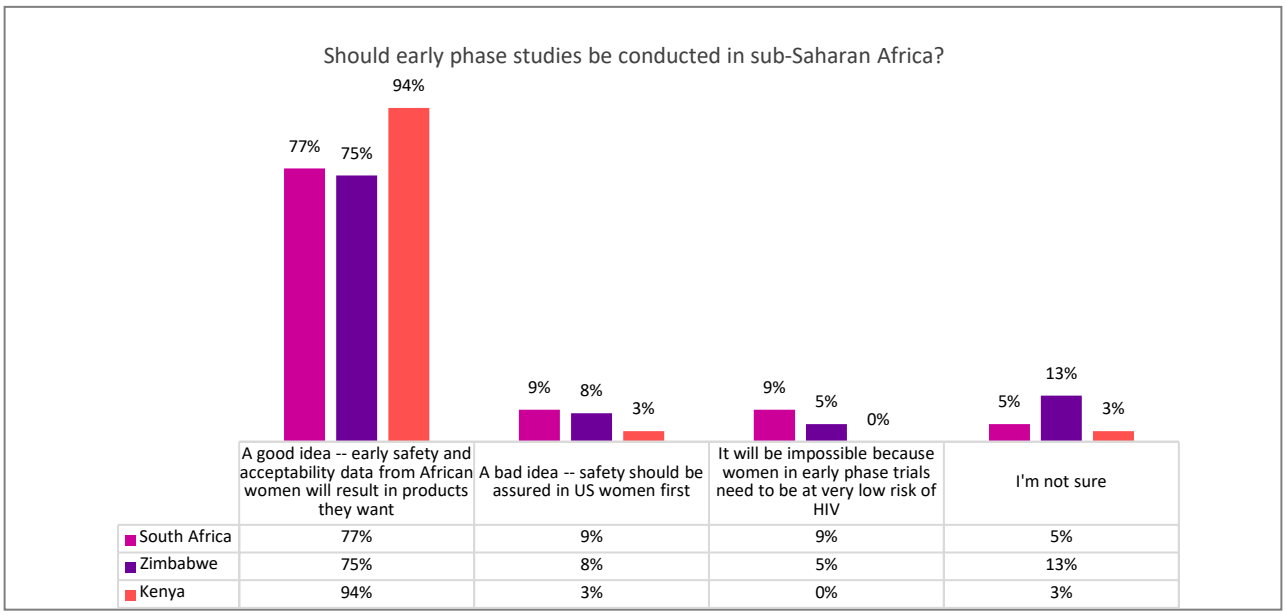
Phase 1 studies typically enroll a relatively small number of participants and involve several tests and procedures – some of them invasive – during a relatively short period of time. Participants need to be generally healthy, not be at risk of acquiring HIV, and, in many studies, also be willing to abstain from sex during the study. Taking part in these studies has few benefits to participants, and, in fact, carries potential risks. For trial sites, ensuring the safety of participants is of utmost concern.

What do stakeholders think?

Stakeholders overwhelmingly agreed that early phase studies should be conducted in Africa, because the safety and acceptability data they will generate may lead to products that African women may actually want and can use. Besides generating data specific to women in the region, participants felt that it would also enhance acceptability of and ownership in the final products because local women had been involved in their development.

Because of all the different tests and procedures and the lengthy study visits (in some cases, taking up an entire day) that trial participants must undergo, not to mention the many sample draws, stakeholders, particularly in Zimbabwe, felt they should receive reimbursement (compensation) at an amount commensurate with the degree of risk involved and level of commitment required of a Phase 1 study. In South Africa, meeting participants asked the CEO of the South African Health Products Regulatory Authority (SAHPRA) to ensure that the new reimbursement schedule for research participants considers Phase 1 trials, not just later phase studies. At each of the meetings there was also much discussion about ensuring the safety of trial participants, and equity in terms of the care and services provided and available to study participants regardless of the site (and country) where they are enrolled. Stakeholders in Zimbabwe were especially concerned that women research participants in Africa would not be treated in the same way as their counterparts in the U.S.

When young women at each of the three meetings were asked if they would take part in early phase and first-in-human studies, some said they would, to advance the science, while others were not comfortable with the potential risks involved.



"If a study is done in North America, then I walk to [CEO's office, National AIDS Control Council] or other people at the Ministry of Health, and I tell them, 'these studies were done in New Zealand, in America, in Canada and we want to use that evidence in Kenya', a policymaker will ask, 'Have there been any studies done on Sub-Saharan Africa?' So, the approval process takes longer."

- Kenneth Ngure, MATRIX End-User Acceptability Co-Lead; Dean, School of Public Health, Jomo Kenyatta University of Agriculture and Technology, Kenya

"I'm not going to own something I was not part of."

- Blossom Makhubalo, Community Engagement Manager, Aurum Klerksdorp Clinical Research Site, South Africa

"Including African women in early phase and FIH trials would be okay if they will also be considered first to benefit from these products if they become available."

- Constancia Mavodza, Research Fellow (Process Evaluations), The Health Research Unit Zimbabwe (THRU ZIM) Zimbabwe

"It is important because it will give a sense of ownership of the final product by African women, having been part of the process from the beginning."

- George Owino, Program Manager, Policy and Advocacy, IAVI; ADVANCE Partner, Kenya

"A woman is the same, whether she's African or American … they have the same needs and duties [as a participant]."

- Adelaide Nyamwanza, Community Advisory Board member, University of Zimbabwe Clinical Research Centre, Zimbabwe

"[I went to join] because I wanted money, the 15$, that was my motive, but when I went there after the discussion I had with the facilitator, I had another point of view from their side" "[…] they gave me all the details required of me to sign on, and I understood more. No, it is not about money, it is something big."

- Omega Chinhoro, former HVTN 107 (Phase 1) trial participant, Zimbabwe

"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, MATRIX Clinical Trials Hub co-lead, Harare Health and Research Centre, Zimbabwe

Views about MATRIX and its approach



Elizabeth Onyango, 2022 AVAC Advocacy Fellow, Kenya

Stakeholders welcomed hearing about the MATRIX project and were enthusiastic about its proposed product line-up and approach to implementation. Participants felt that all too often drugs and other products are introduced without much involvement of the potential end users. Participants commended MATRIX for including potential end-users and other stakeholders early in the research process, as this would increase the chances of having products that were acceptable, affordable, scalable and deliverable. MATRIX was also commended for involving service providers and policymakers at this stage. Participants remarked that if service providers understood how a proposed product worked, they would be able to share information with clients that was accurate rather than potentially contributing to myths and misconceptions about the product.

Including representatives of ministries of health and other policymakers in these early discussions was also lauded, as it would help create champions and establish relationships and understanding of what would be crucial for the progress of the project and its portfolio of products. In South Africa, Hasina Subedar, Senior Technical Advisor, National Department of Health, pointed out that, often, translating products and service delivery models from a clinical trial to actual practice can be difficult, and she challenged the MATRIX team to keep in mind issues around implementation and scale-up as the new products progress through trials.

The stakeholders also commended MATRIX's capacity strengthening initiative to build a pool of qualified local scientists, researchers and research institutions who could conduct early phase and first-in-human studies in the region. At the Kenya meeting, Ruth Laibon-Masha, CEO, National Syndemic Diseases Control Council, observed that for many years there has been limited recognition at the international level of the local scientists who were essential in the conduct of research studies and clinical trials.

It was also greatly appreciated that MATRIX is focusing on products that were women-controlled and that could help overcome service delivery challenges if successful, including products that would require little involvement of service providers.

"I want to congratulate this team because when you start like this [consulting end users], you really begin getting some of these end questions and I hope that we will move forward on that."

- Ruth Laibon-Masha, CEO, National Syndemic Diseases Control Council, Kenya

"I am quite excited about MATRIX and everything you have told us in this meeting, and it is a gamechanger in [HIV prevention] science and technology"

- Sinentlantla Gogela, Ground Force, Advocates for the Prevention of HIV in Africa (APHA), South Africa

"It is really fascinating, these products that are in the pipeline and I hope you will keep us in this journey."

- Mopo Radebe, Technical Officer, HIV Prevention World Health Organization, South Africa

"As a lab scientist, I can say that we tend to think a product is very good but wait until we take it to the end user, and they tell us these things don't work. So, involving end users early when the scientists are just conceiving the idea is very good."

- Daniel Matemo, Study Coordinator, University of Washington/Kenyatta National Hospital, Department of Medical Research, Kenya

"As a potential end user of these products, I'm leaving feeling empowered with a lot of information, and praying that these products will be successful in the trials so that we young women have many choices when it comes to protection."

- Leonidah Ayuma, Advocate and Team Leader, Youth Advisory Champions for Health, Kenya

"Product developers should understand what women want, rather than pushing products just because science shows they are working. We (women) often feel the research community doesn't really care that we are the ones who take these products and sometimes they don't really work. Take community needs and questions seriously. Do women want this?"

- Yvette Raphael, Executive Director, Advocates for the Prevention of HIV in Africa (APHA), South Africa

"… nobody raised their hand when asked if anybody has ever been called to this kind of a meeting before…I love the MATRIX approach, it is important that you are involving the end users early enough in the process ... this a great example of human-centred design."

- Violet Naanyu, Associate Professor, Moi University; AMPATH; member, National Scientific and Ethics Review Committee, Kenya

"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."

- *S*hungu Munyati, Director-General, Biomedical Research & Training Institute, Zimbabwe

"I'm so happy we are seated here because this is the beginning of the process ensuring that us as young women have a say and can help you design products and commodities that will be of use to us … We want to be meaningfully engaged, and most importantly, consistently engaged… At the end of the day, the end users voice matters. Nothing for us without us."

- Jerop Limo, Ambassador for Youth and Adolescents Reproductive Health Programme, Kenya



It's good that MATRIX is considering "the pricing issues … early enough, because many times we talk to communities about new products, then when it is approved, there [are challenges] regarding the prices. When developers are developing these products, they know who they are targeting, so can they just think about pricing as well?"

- Loyiso Saliso, Projects Officer, APHA, South Africa



"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."

- Takunda Sola, HIV Prevention and Key Populations Clinical Officer, Ministry of Health and Child Care, Zimbabwe

"Normally we talk to users when the product is already in the market, and we have to deal with these issues at the end and going back to manufacturers is quite difficult because they've passed the prototype stages and all that. So, sitting in this room I feel like this was a great and timely event, a great opportunity, to sit here and give feedback that will help refine both the products and the research protocols."

- Serah Malaba, Project Director, Strengthening HVST in the Private Sector, Population Services International (PSI), Kenya

Suggestions for MATRIX as it moves forward

The discussions at each of the three meetings gave rise to a number of issues that stakeholders felt the MATRIX project should take into consideration as it moves forward. These are summarized below and include suggestions that may have been described or mentioned in previous sections of this report.

- ***Do not lose sight of the potential market demand and service delivery for these products, including the gaps they will fill.*** While MATRIX is already giving focus to these issues, stakeholders sought to emphasize that the safety and effectiveness of a product were not the only determinants for a product's success.

  > ***"Consider how acceptable these products will be, would they be feasible for implementation? Would there be demand for it? Clear understanding of the community and the product. Also, cost-effectiveness, compared to what else is available – who would benefit from it?"***
  >
  > - Hasina Subedar, Senior Technical Advisor, National Department of Health, South Africa

  > ***"If we focus on the biomedical…and not working together to address the structural issues, we are doing ourselves a disservice.'"***
  >
  > - Dominica Dhakwa, Chief of Party, Zimbabwe Health Interventions, Zimbabwe

- ***Engage with drug regulators and health authorities early*** to understand potential bottlenecks related to drug registration, health policies and service delivery issues. For instance, at the Kenya consultation, one of the meeting participants noted that TAF is not registered in Kenya, which might have implications for the TAF/EVG fast-dissolving insert.

- ***Anticipate and address potential concerns of IRBs/IECs before submitting study protocols for review.*** Because local Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs) may have little or no experience in the review of protocols for early-phase studies, it was recommended that MATRIX researchers request pre-submission meetings with IRB/IECs to provide them with the background for better understanding the rationale for implementing these studies in the region and why they are designed the way they are. Moreover, it was strongly recommended that ***protocols of studies involving placebo products should include an ethical justification or argument for not providing participants with an active product (either as part of the study design or as a standard of prevention).*** Ethicists attending the South Africa and Kenya meetings believed these and other measures, including the possibility of collaborative reviews, would help mitigate the potential for a prolonged IRB/IEC review process and/or the possibility that the protocol would not be approved.

- ***Begin engaging with health care providers early in the product development process and along the way to better ensure buy-in of the product if and when it is approved***. Although MATRIX is focused specifically on early product development, plans must be considered for ensuring there will be ongoing engagement with stakeholders throughout the product development process. As such, MATRIX needs to be thinking about making linkages with other programs who would take responsibility for ensuring ongoing communication with healthcare providers and other key stakeholder groups.

  > ***"Providers play a very important role in either hindering or facilitating the use and availability of some of these products. An example would be for family planning -- if providers don't buy into IUCD, your end user may say that they want the product, but they will not find it anywhere."***
  >
  > - Wilfred Gurupira, Pharmacist, University of Zimbabwe-Clinical Trials Research Centre, Zimbabwe

To this end, the Zimbabwe National Family Planning Council asked how it could work more closely with MATRIX moving forward, citing not only its experience in conducting clinical trials, but more importantly, its understanding of its client's views and preferences regarding different contraceptive methods.

- ***Involve male partners and other key influencers in the design and conduct of trials.*** A woman's male partner can easily influence whether or not she will enroll in a study, but also her adherence to product use and study procedures and whether she remains in the study. Partners can also provide important insight into the acceptability of products from their perspective.

- ***Explore the possible impact that community norms and social change may have on women's sustained use of products*** and identify ways to address these potential barriers. In Kenya, for example, a meeting participant raised the possibility that cultural norms and behaviors regarding menstruation could impede the use of vaginal products.

- ***Temper expectations about the products being evaluated with messages about how the research and development process is a very long and complicated and that, at best, perhaps only one or two products might eventually succeed in trials, be approved and made available.*** A number of stakeholders at the South Africa meeting had initially assumed that all six products being discussed would be introduced – and within a timeframe of just a few years. As they came to realize what MATRIX was all about, they grew especially concerned about the likelihood – and consequences—of these same kinds of misperceptions occurring at the community level. A similar discussion took place in Zimbabwe and recognition that messaging needed to be very clear about the realities of early research and development -- we are only at the beginning of a very long process, and success is not a given. Soon enough, meeting participants were correcting themselves mid-sentence (*'…when this product is approved, I mean, if someday it is potentially approved…'*).

- ***Don't overpromise when it comes to talking about the products:*** While stakeholders appreciated the care taken by presenters, including product developers, to break down the science and explain concepts in terms that were easily understood by all audiences, some felt there were statements made about products that came across as too definitive and overly optimistic.

  > ***"We have to avoid over-promising, over-hyping a product, and be realistic about expectations, because they generate a lot of excitement."***
  >
  > - Yvette Raphael, Executive Director, Advocates for the Prevention of HIV in Africa (APHA), South Africa)

- ***Ensure other key stakeholders are part of the process:*** Stakeholders attending the in-country meetings were eager to continue being a part of MATRIX project activities as they unfold but also recommended that other stakeholders be brought on board whose contribution or support was critical. In South Africa, this included engaging with IRB/IECs, healthcare providers, additional representatives from the National Department of Health and with the National Essential Medicines List Committee, whereas in Kenya, the stakeholders recommended the inclusion of representatives from the drug regulatory authority and the Pharmacy and Poisons Board in future meetings. MATRIX was also urged to include young women in all stakeholder engagements, as they are the future users.

Conclusion and Next Steps

The MATRIX teams thanked stakeholders for the valuable feedback they had contributed at these first meetings and informed them that the information was to be shared with investigators and the product developers. Moreover, stakeholders would be informed regarding how their feedback was received and what changes were or were not being made as a result, and why. Every one of the products in the MATRIX portfolio was seen by participants as potentially important additions to the HIV prevention toolbox, giving women the ability to choose. The remarks and recommendations made regarding specific products will help inform and refine their development as well as the trials that are being planned.

Meeting participants said that the meetings were successful and very informative and hoped they were the beginning of an ongoing process and partnership. They pointed out that few projects, if any, have considered the end user so early in a product's development, and that the MATRIX paradigm will enhance the chances of success in both the innovation and research and development processes. The discussions also contributed greatly to creating understanding about the potential market for the products in the MATRIX portfolio, should they be successful. MATRIX will continue to engage stakeholders as the product development portfolio evolves and continue and to seek their perspectives through various mechanisms, including those suggested during the consultations.

# # #



Annex 1: South Africa Consultation Agenda & Participants List



MATRIX Stakeholders Consultation

Johannesburg, South Africa

5-6 October 2022

DAY 1– Wednesday, 5 October 2022

Time	Session	Title
08:15-09:00		**Registration**
09:00-09:45	**Session 1**	**Welcome and Introductions** ***Nandisile Luthuli Sikwana, Thesla Palanee Phillips,*** ***Orapeleng Motlhaoleng –****NDoH Deputy Director for PrEP Implementation*
CONTEXT AND SETTING THE STAGE		
09:45 -10:15	**Session 2**	**Voices that Matter – and Why** • **Speaking to the HIV prevention needs of young women** ***Chantel Maganye, Sarah Mkhabela*** • **A look at the current HIV prevention landscape** ***Nandisile Luthuli Sikwana***
10:15-10:30	**Session 3**	**MATRIX: Developing the next generation of HIV prevention products for women** ***Thesla Palanee Phillips***
10:30-10-45		**Tea Break**
10:45-11:15	**Session 4**	**Understanding the Research & Development Process** ***Thesla Palanee Phillips*** (15 mins) **Questions and Discussion** (15 mins) Nandisile Luthuli Sikwana - *Facilitator*
11:15-12:00	**Session 5**	**Conducting early phase and first-in-human studies in sub-Saharan Africa** ***Leila E. Mansoor*** (15 mins) **Experiences as a former Phase 1 trial participant** ***Monica Pule*** (5 mins) **Questions and Discussion** (20 mins) Nandisile Luthuli Sikwana - *Facilitator*
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 1		
12:00-13:00	**Session 6**	**Is there a place for new methods and product formulations?** Definate Nhamo, Wawira Nyagah - *Facilitators*
13:00-14:00		**Lunch**
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 2)		
14:00 - 15:30	**Session 7**	**TAF/EVG Fast-Dissolving Insert** • **What is the TAF/EVG Fast-Dissolving Insert?** ***Meredith Clark*** (pre-recorded – 10 minutes) • **MATRIX-001 Phase 1 Study of the TAF/EVG Fast-Dissolving Insert** ***Leila E. Mansoor*** (10 mins) • **Open discussion and interactive session** (75 mins) Nandisile Luthuli Sikwana, Wawira Nyagah - *Facilitators*

Time	Session	Title
15:30-15:45		**Tea Break**
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 3)		
15:45-17:00	**Session 8**	**One-Month Dapivirine Vaginal Film** • **What is the one-month dapivirine vaginal film?** ***Lisa Rohan*** (pre-recorded – 5 minutes) • **MATRIX-002 Acceptability and Safety Study of Two Prototype Vaginal Films** ***Thesla Palanee Phillips*** (10 mins) • **Open discussion and interactive session** (60 mins) Nandisile Luthuli Sikwana and Definate Nhamo - *Facilitators*
17:00-17:05		**Closing Remarks for Day One** ***Thesla Palanee Phillips***
18:30- 21:00		**Reception and Dinner**

DAY 2 – Thursday, 6 October 2022

Time	Session	Title
09:00-09:30	**Session 1**	**Day One Recap and Outstanding Questions** ***Thesla Palanee Phillips*** Nandisile Luthuli Sikwana - *Facilitator*
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 4)		
09:30-10:30	**Session 2**	**Non-Antiretroviral (ARV)/Non-hormonal Contraceptive Multipurpose Vaginal Ring** (Also called the LAMP-IVR) • **What is the non-ARV/non-hormonal contraceptive multipurpose vaginal ring?** ***Marc Baum*** (pre-recorded – 10 minutes) • **Open discussion and interactive session** (50 mins) Definate Nhamo - *Facilitator*
10:30-10-45		**Tea Break**
10:45-11:00	**Session 3**	**Looking farther ahead** • **What is Griffithsin Fast-Dissolving Insert?** ***Lisa Haddad*** (pre-recorded – 5 minutes) • **What are the Cabotegravir Dissolvable Pellet Implants and the Cabotegravir Injectable Depot?** ***Gustavo Doncel*** (pre-recorded – 10 minutes) Imelda Mahaka - *Facilitator*
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 5)		
11:00-11:30	**Session 4**	**A few final questions** Imelda Mahaka, Wawira Nyagah- *Facilitators*
11:30-12:00	**Session 5**	**What do young women think? What do others think?** Wawira Nyagah- *Facilitator*
12-12:45	**Session 6**	**Meeting Evaluation** **Summary and Next Steps** ***Thesla Palanee Phillips, Nandisile Luthuli Sikwana***
13:00-14:00		**Lunch**







MATRIX Stakeholders Consultation

Johannesburg, South Africa

5-6 October 2022

Meeting Participants

Elmari Briedenhann
Technical Head, Programme Engagement
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MOSAIC Partner

Nhlamulo Chantel
Community Liaison Manager
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Denford Chuma
Project coordinator
Pangaea Zimbabwe Aids Trust (PZAT)
MATRIX Stakeholder Engagement

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The Aurum Institute

Sinentlantla Gogela
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Coalition to Accelerate & Support Prevention Research (CASPR) Partner

Jacques Livingston
Biomedical Prevention Specialist
US Agency for International Development (USAID)
South Africa Mission

Gcobisa Madlolo
Young Woman Advocate

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Executive Director
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Chantel Maganye
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Definite Nhamo
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Senior Programme Officer
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Candice Pillay
MATRIX Business Market Dynamics and Commercialization (BACH)
The Aurum Institute

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Former HVTN 086 Phase 1 Study Participant

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Technical Officer, HIV Prevention
World Health Organisation (WHO)

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Wits Reproductive Health and HIV Institute (WRHI)

Yvette Raphael
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Advocates for the Prevention of HIV in Africa (APHA)

Annex 2: Zimbabwe Consultation Agenda & Participants List



MATRIX Stakeholders Consultation

Harare, Zimbabwe

18-19 October 2022

DAY 1– Tuesday, 18 October 2022

Time	Session	Title
08:15-09:00		**Registration**
09:00-09:45	**Session 1**	**Welcome and Introductions** ***Def Nhamo, Nyaradzo Mgodi*** ***Takunda Sola*** *– Clinical Officer, Ministry of Health and Child Care (MoHCC)*
CONTEXT AND SETTING THE STAGE		
09:45 -10:15	**Session 2**	**Voices that Matter – and Why** • **Speaking to the HIV prevention needs of young women** ***Havana Mtetwa, Rosemary Tshuma*** • **A look at the current HIV prevention landscape** ***Def Nhamo***
10:15-10:30	**Session 3**	**MATRIX: Developing the next generation of HIV prevention products for women** ***Nyaradzo Mgodi***
10:30-10-45		**Tea Break**
10:45-11:15	**Session 4**	**Understanding the Research & Development Process** ***Nyaradzo Mgodi*** *(*15 mins) **Questions and Discussion** (15 mins) Def Nhamo - *Facilitator*
11:15-12:00	**Session 5**	**Conducting early phase and first-in-human studies in sub-Saharan Africa** ***Nyaradzo Mgodi*** (15 mins) **Experiences as a former Phase 1 trial participant** ***Omega Chinhoro, Judith Mukute*** (5 mins) **Questions and Discussion** (20 mins) Def Nhamo - *Facilitator*
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 1)		
12:00-13:00	**Session 6**	**Is there a place for new methods and product formulations?** Wawira Nyagah - *Facilitator*
13:00-14:00		**Lunch**
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 2)		
14:00 - 15:30	**Session 7**	**TAF/EVG Fast-Dissolving Insert** • **What is the TAF/EVG Fast-Dissolving Insert?** ***Meredith Clark*** (pre-recorded – 10 minutes) • **MATRIX-001 Phase 1 Study of the TAF/EVG Fast-Dissolving Insert** ***Nyaradzo Mgodi*** (10 mins)

Time	Session	Title
		• **Open discussion and interactive session** (75 mins) Nandisile Luthuli Sikwana - *Facilitator*
15:30-15:45		**Tea Break**
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 3)		
15:45-17:00	**Session 8**	**One-Month Dapivirine Vaginal Film** • **What is the one-month dapivirine vaginal film?** ***Lisa Rohan*** (pre-recorded – 5 minutes) • **MATRIX-002 Acceptability and Safety Study of Two Prototype Vaginal Films** ***Nyaradzo Mgodi*** (10 mins) **Experience as a former placebo trial participant** ***Nyarai Moyo*** (5 mins) • **Open discussion and interactive session** (60 mins) Nandisile Luthuli Sikwana and Wawira Nyagah - *Facilitators*
17:00-17:05		**Closing Remarks for Day One** ***Nyaradzo Mgodi***
18:30- 21:00		**Reception and Dinner**

DAY 2 – Wednesday, 19 October 2022

Time	Session	Title
09:00-09:30	**Session 1**	**Day One Recap and Outstanding Questions** ***Nyaradzo Mgodi*** Def Nhamo - *Facilitator*
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 4		
09:30-10:30	**Session 2**	**Non-Antiretroviral (ARV)/Non-hormonal Contraceptive Multipurpose Vaginal Ring** (Also called the LAMP-IVR) • **What is the non-ARV/non-hormonal contraceptive multipurpose vaginal ring?** ***Marc Baum*** (pre-recorded – 10 minutes) • **Open discussion and interactive session** (50 mins) Definate Nhamo - *Facilitator*
10:30-10-45		**Tea Break**
10:45-11:00	**Session 3**	**Looking farther ahead** • **What is Griffithsin Fast-Dissolving Insert?** ***Lisa Haddad*** (pre-recorded – 5 minutes) • **What are the Cabotegravir Dissolvable Pellet Implants and the Cabotegravir Injectable Depot?** ***Gustavo Doncel*** (pre-recorded – 10 minutes) Nandisile Luthuli Sikwana - *Facilitator*
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 5)		
11:00-11:30	**Session 4**	**A few final questions** Nandisile Luthuli Sikwana - *Facilitator*
11:30-12:00	**Session 5**	**What do young women think? What do others think?** Wawira Nyagah – *Facilitator* **Key highlights from end-user consultations** ***Def Nhamo*** (10 mins) Discussion
12-12:45	**Session 6**	**Meeting Evaluation** **Summary and Next Steps** ***Nyaradzo Mgodi, Def Nhamo, Takunda Sola*** *(MoHCC)*
3:00-14:00		**Lunch**

MATRIX Stakeholders Consultation

Harare, Zimbabwe

18-19 October 2022

Meeting Participants

Gwendoline Chapwanya
Project Coordinator
Pangaea Zimbabwe AIDS Trust (PZAT)

Charles Chasakara
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Lutheran Community of Southern Africa

Munyaradzi Chimwara
Project Lead
Advocacy Core Team (ACT)

Omega Chinhoro
Former Phase 1 Trial Participant
HVTN 107

Liberty Chirinda
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Onward Chironda
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Fortunate Chiwamba
Community Facilitator-Female Sex Workers
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Denford Chuma
MATRIX Project Coordinator
Pangaea Zimbabwe AIDS Trust (PZAT)

Dominica Dhakwa
Chief of Party
Zimbabwe Health Interventions (ZHI)

Rumbidzai Filips
Former Trial Participant
REACH (MTN-034)

Wilfred Gurupira
Pharmacist
University of Zimbabwe Clinical Trials Research Centre (UZ-CTRC)

Gladys Gwatidzo
Former Trial Participant
REACH (MTN-034)

Wilbert Ishemunyoro
Research Assistant
University of Zimbabwe Clinical Trials Research Centre (UZ-CTRC)

Teclar Jaji
Community Facilitator- Female Sex Workers
Zim-TTECH

Talent Jumo
Founder and Director
Katswe Sistahood

Jacqueline Kabongo
Research Coordinator
Pangaea Zimbabwe AIDS Trust (PZAT)

Mavis Kambiro
Community Advisory Board Member
University of Zimbabwe Clinical Trials Research Centre (UZ-CTRC)

Cuthbert Kapingura
Nurse
Marlborough Clinic

Chido Kaseke
Nurse
Wilkins Hospital

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Annex 3: Kenya Consultation Agenda & Participants List



MATRIX Stakeholders Consultation

Nairobi, Kenya

8-9 November 2022

DAY 1 – Tuesday, 8 November 2022

Time	Session	Title
08:15-09:00		**Registration**
09:00-09:45	**Session 1**	**Welcome and Introductions** ***Wawira Nyagah, Dr. Nelly Mugo,*** ***Dr. Ruth Laibon-Masha*** - *CEO, National Syndemic Disease Control Council (NSDCC)*
CONTEXT AND SETTING THE STAGE		
09:45 -10:15	**Session 2**	**Voices that Matter – and Why** • **Speaking to the HIV prevention needs of young women** ***Margaret Kirigo, Jerop Limo, Margaret Akinyi Atieno*** • **A look at the current HIV prevention landscape** ***Daisy Ouya***
10:15-10:30	**Session 3**	**MATRIX: Developing the next generation of HIV prevention products for women** ***Dr. Nelly Mugo***
10:30-10-45		**Tea Break**
10:45-11:15	**Session 4**	**Understanding the Research & Development Process** ***Dr. Nelly Mugo*** (15 mins) **Questions and Discussion** (15 mins) Wawira Nyagah - *Facilitator*
11:15-12:00	**Session 5**	**Conducting early phase and first-in-human studies in sub-Saharan Africa** ***Prof. Kenneth Ngure*** (15 mins) **Experiences as a former Phase 1 trial participant** ***Steve Anguva*** (5 mins) **Views and concerns regarding early phase and first-in-human studies in SSA** ***Prof. Violet Naanyu*** (5 mins) **Questions and Discussion** (20 mins) Daisy Ouya - *Facilitator*
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 1)		
12:00-13:00	**Session 6**	**Is there a place for new methods and product formulations?** Wawira Nyagah - *Facilitator*
13:00-14:00		**Lunch**
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 2)		
14:00 - 15:30	**Session 7**	**TAF/EVG Fast-Dissolving Insert** • **What is the TAF/EVG Fast-Dissolving Insert?** ***Meredith Clark*** (pre-recorded – 10 minutes) • **MATRIX-001 Phase 1 Study of the TAF/EVG Fast-Dissolving Insert** ***Prof. Kenneth Ngure*** (10 mins) • **Open discussion and interactive session** (75 mins) Definate Nhamo - *Facilitator*

Time	Session	Title
15:30-15:45		**Tea Break**
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 3)		
15:45-17:00	**Session 8**	**One-Month Dapivirine Vaginal Film** • **What is the one-month dapivirine vaginal film?** ***Lisa Rohan*** (pre-recorded – 5 minutes) • **MATRIX-002 Acceptability and Safety Study of Two Prototype Vaginal Films** ***Dr. Nelly Mugo*** (10 mins) • **Open discussion and interactive session** (60 mins) Wawira Nyagah - *Facilitator*
17:00-17:05		**Closing Remarks for Day One** ***Dr. Nelly Mugo***
18:30- 21:00		**Reception and Dinner**

DAY 2 – Wednesday, 9 November 2022

Time	Session	Title
09:00-09:30	**Session 1**	**Day One Recap and Outstanding Questions** ***Dr. Nelly Mugo*** Wawira Nyagah - *Facilitator*
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 4)		
09:30-10:30	**Session 2**	**Non-Antiretroviral (ARV)/Non-hormonal Contraceptive Multipurpose Vaginal Ring** (Also called the LAMP-IVR) • **What is the non-ARV/non-hormonal contraceptive multipurpose vaginal ring?** ***Marc Baum*** (pre-recorded – 10 minutes) • **Open discussion and interactive session** (50 mins) Definate Nhamo - *Facilitator*
10:30-10-45		**Tea Break**
10:45-11:00	**Session 3**	**Looking farther ahead** • **What is the Griffithsin Fast-Dissolving Insert?** ***Lisa Haddad*** (pre-recorded – 5 minutes) • **What are the Cabotegravir Dissolvable Pellet Implants and the Cabotegravir Injectable Depot?** ***Gustavo Doncel*** (pre-recorded – 10 minutes) Imelda Mahaka - *Facilitator*
SEEKING STAKEHOLDERS' VIEWS AND PERSPECTIVES (PART 5)		
11:00-11:30	**Session 4**	**A few final questions** Denford Chuma- *Facilitator*
11:30-12:00	**Session 5**	**What do young women think? What do others think?** Jacque Wambui - *Facilitator*
12-12:45	**Session 6**	**Meeting Evaluation** **Summary and Next Steps** ***Prof. Kenneth Ngure, Wawira Nyagah***
13:00-14:00		**Lunch**

MATRIX Stakeholders Consultation

Nairobi, Kenya

8-9 November 2022

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For more information about MATRIX, please go to www.matrixr4prevention.org

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