MATRIX

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

2023 (Year 2)

Regulatory and Product Development Stakeholder Consultation

1 September 2023 ■ Johannesburg, South Africa

FINAL REPORT

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

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

United States Agency for International Development (USAID) Cooperative Agreement Number 7200AA22CA00002

MATRIX 2023 (Year 2) Regulatory and Drug Development Stakeholder Consultation Final Report, 10 January 2024

Suggested citation: MATRIX, a USAID Project to Advance the Research and Development of Innovative HIV Prevention Products for Women 2023 Regulatory and Drug Development Stakeholder Consultation Final Report. January 2024

For more information on MATRIX and its activities, please visit www.matrix4prevention.org

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Acknowledgments

The Regulatory and Drug Development Consultation was conducted as an activity of MATRIX, a USAID project to advance the research and development of innovative HIV prevention products for women. MATRIX's Design to Delivery (D2D) Pillar 3 (Stakeholder Engagement) was responsible for developing the original concept for this consultation, setting the objectives and sending invitations. With MATRIX's reorganization of D2D, responsibility for stakeholder engagement shifted to Prime, and as such, the remaining tasks related to this consultation, including development of the agenda and other content, were carried out by Prime and coordinated by Lisa Rossi. Special thanks to the Pillar 3 team for setting a solid foundation that made Prime's work all the more easy: Leonard Solai (Population Council/IPM South Africa), the Pillar 3 co-lead for Prime; Nandisile Luthuli-Sikwana (AVAC), co-lead for South Africa; Definate Nhamo (Pangaea Zimbabwe AIDS Trust, or PZAT) co-lead for Zimbabwe; Daisy Ouya (AVAC) the co-lead for Kenya; as well as other Pillar 3 members: Sinazo Pato (Population Council/IPM South Africa); PZAT's Wanzirai Makoni, Imelda Mahaka and Francis Simmonds, and from AVAC, Mitchell Warren and Stacey Hannah.

Their continued support during and even after the transition contributed to the success of the consultation. In particular, Definate Nhamo and Daisy Ouya are to be thanked for their meticulous follow-up and personal communications with Zimbabwe and Kenya stakeholders.

Leonard Solai, as well as Jim Turpin (Prime), Jeremy Nuttall (Population Council) and Shabir Baboo (Right to Care, South Africa), a member of MATRIX's independent Scientific Advisory Group, provided valuable input regarding the agenda, and in particular, helped frame the specific questions to ask of stakeholders during the discussion periods. Their advice and counsel resulted in Sharon Hillier (Magee-Womens Research Institute – MWRI), MATRIX Executive Director; and MATRIX Deputy Director Thesla Palanee-Phillips (Wits RHI) being able to facilitate a more rich and meaningful discussion.

Additionally, credit goes to the product developers who provided succinct and informative overviews of their products – Gustavo Doncel and Melissa Peet (CONRAD), Lisa Rohan (University of Pittsburgh/MWRI, Lisa Haddad (Population Council) and John Moss (Oak Crest Institute for Science), not to mention Nyaradzo Mgodi (Harare Health and Research Consortium -HHRC); Leila Mansoor (Centre for AIDS Programme of Research in South Africa – CAPRISA) and Kathryn Mngadi (Aurum Institute), for their presentations on product-related studies; and Nyaradzo Mgodi and Kenneth Ngure (Jomo Kenyatta University of Agriculture and Technology) for moderating some of these sessions.

Thanks to Vivienne Naidoo for her expert management and oversight of travel and logistics, hotel and meeting arrangements, including the welcome dinner and closing reception. Her attention to detail is unmatched.

Most importantly, we wish to thank all stakeholders –those who in person and virtually – for their valuable contributions to the discussion and giving MATRIX much to think about as it continues its work and mission.

Lastly, we wish to thank USAID, and in particular, Shannon Allen, Chelsea Solmo, Antoinette Nelson and Mary Latka for recognizing the value and importance of stakeholder engagement as an essential component of MATRIX.

This report was written by Lisa Rossi, MWRI, communications director for MATRIX and part of the MATRIX Prime team, based in large part on a transcript of the meeting prepared by Vivian Naidoo and additional notetaking by Definite Nhamo, Wanzirai Makoni and Francis Simmonds . As could be expected, Ariane van der Straten (Prime) proved herself to be astute proof-reader and editor. ■

Photo Credits: Lisa Rossi, MATRIX

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Acronyms and Abbreviations

AMRH	African Medicines Regulatory Harmonization (Initiative)
API	Active Pharmaceutical Ingredient
ART	Antiretroviral Therapy
ARV	Antiretroviral
AU	African Union
AUDA-NEPAD	African Union Development Agency-NEPAD
AVAREF	African Vaccine Regulatory Forum
BRTI	Biomedical Research & Training Institute
CAB-LA	Cabotegravir long-acting injectable
CAPRISA	Centre for the AIDS Programme of Research in South Africa
CASPR	Coalition to Accelerate and Support Prevention Research
CTD	Common Technical Document
CRS	Clinical Research Site
DVR	Dapivirine Vaginal Ring
ECVP	Evidence Considerations for Vaccine Policy
EMA	European Medicines Agency
FDA	U.S. Food and Drug Administration
HHRC	Harare Health and Research Consortium
HIV	Human immunodeficiency virus
HPV	Human Papillomavirus
HSV	Herpes Simplex Virus
HSV-2	Herpes Simplex Virus -2
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
IoR	Investigator of Record
IPRP	International Pharmaceutical Regulators Programme
IRB	Institutional Review Board
KEMRI	Kenya Medical Research Institute
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
NEPAD	New Partnership for Africa's Development (an agency of the African Union)
NSDCC	National Syndemic Diseases Control Council
PD	Product Developer
PEP	Post-Exposure Prophylaxis
PEPFAR	United States President's Emergency Plan for AIDS Relief
PI	Principal Investigator
PK	Pharmacokinetics
PrEP	Pre-Exposure Prophylaxis
PZAT	Pangaea Zimbabwe AIDS Trust
R&D	Research and Development
SADAC	Southern African Development Community
SAHPRA	South African Health Products Regulatory Authority
STI	Sexually Transmitted Infection
TAF/EVG	Tenofovir alafenamide (TAF)/elvitegravir (EVG)
TB	Tuberculosis
TMDA	Tanzania Medicines & Medical Devices Authority
UKZN	University of KwaZulu Natal
USAID	United States Agency for International Development
WHO	World Health Organization


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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 currently taking place in Kenya, South Africa, the United States and Zimbabwe and being carried out by 19 partners from both the Global North and Global South. Part and parcel to MATRIX's mission is a commitment to strengthening the research and development capacity of African investigators.

Clariator Mvurume, Senior Regulatory Officer in the Evaluations and Registration Division at the Medicines Control Authority of Zimbabwe (MCAZ).

A key feature of the MATRIX paradigm is also its focus on being responsive to end-user and stakeholder feedback during the earliest stages of product development in order 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, Zimbabwe and Kenya to seek stakeholders' feedback on the MATRIX mission and its pipeline of products. Consultations were attended by a wide range of stakeholders, including policymakers, advocates, civil society, healthcare providers, regulators, ethicists, implementers, former study participants, adolescent girls and young women, among others. While the input received through these first consultations was invaluable, as MATRIX moved into its second year it became evident that a more focused conversation on regulatory processes would be of benefit to MATRIX, and in particular, its product developers.

As such, MATRIX convened the Regulatory and Product Development Stakeholders Consultation on 1 September 2023 at the Southern Sun Rosebank, Johannesburg, South Africa. The objectives of the consultation were to:

- Seek guidance on preferred mechanisms of engagement both now, i.e., early in the development of products, and as products advance;
- Understand country-level and regional priorities regarding the development of HIV prevention products for women, including dual-purpose products for both prevention of HIV and pregnancy.

The consultation was attended by 36 stakeholders – 31 in-person and five virtual attendees – representing regulatory authorities, ministries of health, ethics committees (ECs) and other policy makers from Kenya (7), South Africa (15) and Zimbabwe (12), as well regional/international bodies, namely, the African Union Development Agency (AUDA-NEPAD) and the Medicines Patent Pool. Some of the meeting's participants had taken part in one of MATRIX's earlier in-country stakeholder consultations. Also in attendance were several MATRIX partners, including representatives from each of the four product developers. (See Annex 2 for the list of meeting participants and their bios.)

The agenda was structured to allow ample time for discussion about MATRIX's mission and approach regarding early research and development and, more specifically, its current portfolio of nine products. Three sessions were expressly for the purpose of soliciting feedback to questions pertaining to 1) MATRIX products that contain existing active pharmaceutical ingredients (APIs), 2) those containing novel agents and 3) dual-purpose products being developed for the prevention of both HIV and pregnancy There were overarching questions as well.

The first question asked was whether mechanisms existed through which product developers could engage with regulatory authorities about products still in pre-clinical research, and such mechanisms do exist within the South African Health Products Regulatory Authority (SAHPRA) and Medicines Control Authority of Zimbabwe (MRCZ). It could not be established if the same was true for Kenya, as there were no representatives in attendance from the Pharmacy and Poisons Board. Zazibona, a regional structure for reliance which includes MATRIX countries, has no such mechanism, but it's quite likely that the African Medicines Agency (AMA) will have a mechanism for early engagement once it is fully operational, though when this might be was uncertain. The AMA was established as a specialized agency of the African Union (AU) to enhance capacity for regulation of medical products in order to ensure access to quality, safe and effective products on the continent.

The African Vaccine Regulatory Forum (AVAREF) was mentioned as a potential vehicle for early engagement around clinical trials. AVAREF is a network of African national regulatory authorities and ethics committees that conducts joint

reviews of clinical trials and uses harmonization and reliance as pillars for capacity building. Founded by the World Health Organization (WHO), its focus is no longer just vaccines, and it now serves as a technical committee for African Medicines Regulatory Harmonization (AMRH) initiative. Stakeholders also recommended early engagement take place with ethics committees and Ministries of Health. Indeed, stakeholders cautioned that even if MATRIX and its product developers were to pursue regional or continental mechanisms like AVAREF and the AMA, it would still be important to engage at the country-level and imperative that MATRIX activities align with national plans and priorities.

Other advice for product developers, especially those working on products based on existing APIs such as dapivirine and cabotegravir, which are used in methods already approved for HIV prevention, was that they be able to demonstrate the potential added value of these new products and what the cost of that value may be compared existing modalities. While there was interest in products containing novel agents, i.e., non-antiretroviral (ARV) drugs, product developers were advised to temper messaging about their possible benefits. For instance, just because they're not used for the treatment of HIV doesn't mean HIV testing would not be required prior to and during use. HIV testing will be given in the delivery of any HIV prevention product. There was also much interest in the dual-purpose products being developed under MATRIX, and stakeholders were eager to take part in future deliberations focused on regulatory guidance and clinical trial design considerations.

Peter Arimi, Program Director of the HIV Prevention Technical Support Unit (HIV TSU) of Partners for Health and Development in Africa (PHDA) , Kenya.. Seated next to him is Betsy Tolley of FHI 360, co-lead of End-User Product Preferences Research, a Pillar within MATRIX's Design to Delivery Hub.

It was an interesting time to be convening stakeholders for a discussion of this kind. The African regulatory framework is undergoing immense changes as it seeks to become more independent, a process that has been years in the making. Structures focused on collaborative mechanisms, harmonization and reliance that were established in part to build capacity have already made significant progress. After COVID-19, seeing that product development and manufacturing can be done on the African continent is also now a priority. Indeed, a commitment to bring about change was evident throughout the consultation. A lively discussion ensued when stakeholders were asked how MATRIX could keep in step with the evolving structures and collaborative mechanisms while still having to follow a development pathway defined by the US Food and Drug Administration (FDA). There was clear consensus that a process involving the FDA – at least in its current form – does not serve the needs of African populations. Besides, the idea is to get away from reliance on entities like the FDA and the European Medicines Agency – it was time that individual regulatory authorities and/or an Africa-wide regulatory system, i.e., the AMA, are able to make their own decisions about and in the best interest of the people of Africa. As such, stakeholders urged MATRIX and its product developers to find ways to work with the AMA, either in parallel or in collaboration with the FDA.

Many of the questions being asked served only to raise new ones. For MATRIX, the consultation provided important insight but also demonstrated that there is still much to learn and to better understand. While MATRIX's mission and objectives are in keeping with and supportive of the paradigm shift taking place in Africa, MATRIX is at the same time married to processes that are dictated by and/or beholden to U.S. values. Clearly, more discussion will be required. One suggestion was that AUDA-NEPAD, as a neutral party, convene a meeting, which it was suggested MATRIX sponsor Such a meeting would help provide more clarity for how MATRIX product developers should be working with the African Medicines Authority (AMA) and national regulatory authorities, both now and as these structures mature – a discussion of great relevance to other research organizations and product developers as well.

As MATRIX products advance through the research and development process, this new system – the AMA – will also be maturing. There may be ways that MATRIX can contribute to the success of these efforts. The fact that MATRIX is conducting Phase 1 trials in Africa – in addition to the US – was in and of itself seen as a learning opportunity for regulators, research ethicists and policy makers.

Of note, MATRIX is planning to hold its next stakeholder meeting in Nairobi (late August/early September 2024). Special effort will be made to engage with representatives from Kenya's Pharmacy and Poisons Control Board, who were not in attendance at the last consultation, and to ensure their participation in larger and future discussion as well.

Engagement with stakeholders this early in the research and development process is not the norm. In her introduction, Sharon Hillier acknowledged as much, calling the consultation "an experiment in early drug development," one in which the feedback of regulators and policy makers could actually make a real difference. Stakeholders were eager participants in the day's discussions and excited to take the conversation forward as MATRIX, its products and the African regulatory framework evolve. ■

About this Report

As with the consultations's agenda, which can be found in Annex 1, this report begins with two sections that intend to set the stage and provide context for later discussions, the first being an overview of the current and evolving HIV prevention landscape (*see* p. 12), and the second, an overview of MATRIX's mission, structure and product portfolio (*see* pages 13-14). For the purposes of this report, the section that follows provides more in-depth information about each of the nine products, including dual-purpose products for the prevention of both HIV and pregnancy, and where relevant, related studies, grouped according to whether they contain existing active pharmaceutical ingredients (API) or novel agents (*see* pages 15-19)

Stakeholder feedback received during the three discussion sessions is summarized on pages 20-28, including to specific questions regarding MATRIX's overall approach and considerations that may be unique or of particular importance to different categories of products, namely those with existing APIs, those containing novel agents and dual-purpose products. Additional insight and recommendations are summarized as well. The report concludes with "Reflections and Next Steps" (*see* pages 29-30).

As mentioned above, the meeting agenda is provided in Annex 1. The list of meeting participants and brief bios can be found in Annex 2. ■

Lillian Omutoko member of the National Scientific Ethics Research Committee, Kenyatta National Hospital-University of Nairobi Ethics Research Committee; Bioethics Society of Kenya; Research Ethics Association of Southern Africa and Africa Bioethics Consortium.

The Current and Evolving HIV Prevention Landscape

Despite major advances in HIV prevention and treatment, the global burden of HIV remains unacceptably high. According to 2023 estimates from UNAIDS and the World Health Organization, approximately 39 million people are currently living with HIV, 54 percent of whom are women and girls. In sub-Saharan Africa, six of seven new HIV infections among adolescents aged 15–19 years are among girls.

Daily oral PrEP (pre-exposure prophylaxis), which requires taking an antiretroviral (ARV) tablet every day is the only biomedical prevention method generally available in Africa. No single approach can be expected to stop the HIV pandemic. A range of different options is needed to meet the diverse and changing needs of individuals at risk for HIV infection. No matter how effective a product may be, it cannot provide protection if not used. With oral PrEP, for example, not everyone finds taking a daily pill to be easy. For some, it may be the side effects or the stigma associated with taking an ARV that may be deterrents.

A monthly vaginal ring may appeal to women wanting a more discreet method, and one that delivers drug locally inside the vagina rather than systemically throughout the body. The monthly dapivirine vaginal ring 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. A three-month dapivirine ring is also being developed. 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 also been recommended by WHO as an additional HIV prevention option.

Both the dapivirine ring and CAB-LA have been approved or are under regulatory review in several African countries, including in Kenya, South Africa and Zimbabwe. Yet, at present, the only means of access to either or both products are through a study called CATALYST— Catalyzing access to new prevention products to stop HIV – which is being conducted by the USAID-funded MOSAIC (Maximizing Options to Advance Informed Choice for HIV Prevention) program. CATALYST is taking place at 28 sites in five countries, namely in Kenya, Lesotho, South Africa, Uganda and Zimbabwe.

Other biomedical HIV prevention options are being evaluated in late-phase clinical trials, including a subcutaneous injection given just under the skin every six months (lenacapavir), another daily oral PrEP pill (emtricitabine and tenofovir alafenamide) and the dual prevention pill (tenofovir disoproxil fumarate and emtricitabine, and levonorgestrel and ethinyl estradiol. With the exception of the three-month dapivirine ring, all involve systemic delivery of an antiretroviral (ARV) drug and are either pills or injections. Additional options are needed, including non-systemic products that can concentrate drug at the route of exposure (e.g., the vagina) and products that would be used on-demand, at the time of sex.

The best product is the one an individual can use effectively when needed, which is why choice is important, because the more options that are available, the more likely the preferred option can and will be used. ■

About MATRIX

MATRIX is a five-year program funded by the U.S. Agency for International Development (USAID) that aims to expedite the research and development of HIV prevention products for women – including products designed to protect against both HIV and pregnancy – that in addition to being safe and effective, will be **acceptable**, **affordable**, **scalable** and **deliverable** in the settings where they are needed most. MATRIX stands for **M**icrobicide R&D to **A**dvance HIV Prevention **T**echnologies through **R**esponsive **I**nnovation and e**X**cellence.

MATRIX activities are focused on the ***early*** research and development of products, which involves both pre-clinical research – the laboratory and animal studies needed to support a product's evaluation in humans – and the first clinical trials of products. Through its North-South Partnerships, MATRIX also aims to strengthen the research and development capacity of African investigators to facilitate full and sustainable ownership of this work into the future.

Diversity is the hallmark of the MATRIX pipeline of products, which includes those designed to provide protection for six months to a year; on-demand vaginal products meant to be used around the time of sex; and vaginal products that would be used for a month at a time. Some products are new formulations of existing antiretroviral (ARV)-based methods, while others contain novel antiviral agents. Of the nine HIV prevention products being developed under MATRIX, four are dual-purpose products for prevention of both HIV and pregnancy. Most have not yet been tested in clinical trials.

Early research and development is inherently risky. Of hundreds of potential products being evaluated in pre-clinical research, only a handful will make it into early-phase clinical studies, and fewer still can be expected to progress all the way to regulatory approval. MATRIX hopes to improve the odds of success for its products by ensuring only the most promising products advance from pre-clinical research to early phase testing -- products that not only laboratory and animal studies suggest will be safe and effective in humans but that end-users also indicate they are likely to use; products that could be manufactured and distributed locally at low cost and minimal burden on healthcare systems; and products that meet the requirements of Ministries of Health and national HIV prevention programs.

MATRIX is unique in that it seeks to integrate end-users' and stakeholders' feedback early in the process to inform decisions about product design and overall research priorities. MATRIX also intends to conduct placebo studies and early phase (Phase 1) clinical trials in Africa – not just in the US – to obtain important data on the safety and acceptability of new products in the populations of women that matter most.

MATRIX is co-led by Sharon Hillier, Ph.D., of Magee-Womens Research Institute (MWRI) and the University of Pittsburgh School of Medicine, USA, with Thesla Palanee-Phillips, Ph.D., from Wits RHI and University of Witwatersrand, South Africa, serving as deputy director. MATRIX is being implemented in collaboration with 19 partner organizations based in Kenya, South Africa, the United States and Zimbabwe that, collectively, have expertise across multiple fields, including drug formulation, drug delivery and product development; clinical trials design and implementation; human-centered design and socio-behavioral research; market strategy and business case development; capacity strengthening; and stakeholder engagement.

The Five Activity Hubs of MATRIX

Technology Accelerator

- Manages development process of products, and with input of an independent **Scientific Advisory Group**, advises on a product's next steps
- Provides support to other research and development endeavors through seed funding and other grants, including of projects led by African investigators

Clinical Trials

- Oversees design and implementation of placebo studies and Phase 1 trials of products at partner clinical trial sites in the U.S., Kenya, South Africa and Zimbabwe

Design to Delivery (D2D)

- Conducts end-user research to understand women's and stakeholders' preferences for products and product attributes
- Designs and implements behavioral studies & socio-behavioral research within trials

Business, Market Dynamics and Commercialization (BACH)

- Conducts business case & market analysis; seeks linkages with possible investors

Capacity Strengthening, Engagement and Mentorship (CaSE)

- Matches African investigators with mentorship and fellowship opportunities, with an emphasis on early R&D

Among its partners are four Product Developers (PDs) – all based in the United States: CONRAD, a non-profit organization affiliated with the Eastern Virginia Medical School; Oak Crest Institute for Science; Population Council; and the University of Pittsburgh, MWRI. Partnering with MATRIX in the conduct of clinical trials are five sites in Africa (in Kenya, South Africa and Zimbabwe) and two sites in the United States. African sites include the Kenya Medical Research Institute (KEMRI); in South Africa, the Aurum Institute, Centre for the AIDS Programme of Research in South Africa (CAPRISA) and Wits RHI; and in Zimbabwe, the Harare Health and Research Consortium (HHRC). MATRIX's U.S. sites are affiliated with the Eastern Virginia Medical

Center in Norfolk, Va., and MWRI/University of Pittsburgh. The MATRIX structure consists of five activity hubs (see inset) that support the product developers and overall mission of MATRIXRHI

The following table provide a snapshot of the products being developed through MATRIX and **their status at the time of the consultation** (1 Sept. 2023). (*See next section for additional information about each of these products.*) ■

MATRIX Product Pipeline: A snapshot

		Product	Developer	Product Type	Active ingredient(s)	How used	Protection goal	Unique features/ Additional Information	Development Status
		Products for Prevention of HIV							
1		**TAF/EVG Fast-dissolving vaginal insert**	**CONRAD** (USA)	**Fast-dissolving insert**	**TAF/EVG** *tenofovir alafenamide & elvitegravir* *NRTI & integrase inhibitor (ARVs)*	**On-demand** (women insert themselves at or around time of sex)	**Up to 3 days**	MATRIX is evaluating product for its primary indication to prevent HIV. TAF has also shown activity against HSV, which could be added benefit. CONRAD also evaluating the insert's rectal use.	**MATRIX-001** to evaluate safety and acceptability of insert in 60 women at 3 sites in Kenya, South Africa and US–the first Phase 1 study in African women. Expected start 2023.
2		**Griffithsin Fast-dissolving vaginal insert**	**Population Council** (USA)	**Fast-dissolving insert**	**Griffithsin antiviral protein (non-ARV)** *Viral entry inhibitor*	**On-demand** (women insert themselves at time of sex)	**4-8 hours**	MATRIX is evaluating the insert for its primary indication for prevention of HIV. Animal and laboratory studies indicate Griffithsin to also have activity against HPV and HSV	Pre-clinical
3		**Dapivirine vaginal film**	**Univ of Pittsburgh** (USA)	**Vaginal film**	**Dapivirine** *NNRTI (ARV)*	**Women insert themselves**	**1 month**	Film would slowly release drug until it completely dissolves. *Also being developed as a dual-purpose product (see below)*	First trial of a monthly film, **MATRIX-002** to evaluate acceptability, usability of 2 placebo films at 5 sites in Kenya, South Africa, Zimbabwe and US. Expected start 2023. To determine film for first-in-human trial of monthly dapivirine film.
4		**Cabotegravir hydrogel injectable**	**CONRAD** (USA)	**Injectable depot**	**Cabotegravir** *Integrase strand inhibitor (ARV)*	**Injection given under the skin**	**4-6 months**	Initially a liquid, hydrogel forms into a small ball that would slowly release drug as it dissolves. (If needed, could be removed in first month) *Also being developed as dual-purpose product (see below)*	**Pre-clinical**
5		**Cabotegravir dissolvable pellets**	**CONRAD** (USA)	**Pellet implant**	**Cabotegravir** *Integrase strand inhibitor (ARV)*	**Inserted under skin**	**Up to 1 year**	8-9 pellets would be inserted in a row; pellets slowly release drug as they dissolve over course of a year. (If needed, removable in first 1-2 months) *Also being developed as dual-purpose product (see below)*	**Pre-clinical**
		Products for Prevention of HIV and Pregnancy (Dual Purpose)							
1		**Non-ARV/ nonhormonal contraceptive dual-purpose vaginal ring**	**Oak Crest Inst of Science** (USA)	**Vaginal ring**	**Antiviral peptide (non-ARV)** *(protein fragment)* **Non-hormonal contraceptive** *A soluble Adenylate Cyclase (sAC) inhibitor -affects sperm's ability to move, fertilize eggs*	**Women insert themselves**	**1 month**	MATRIX is evaluating the ring for its primary indications to prevent HIV and pregnancy. The antiviral also shows activity against HSV and HPV, which could be an added benefit.	**MATRIX-003** to evaluate acceptability of 2 placebo vaginal rings as precursor to a study of the active ring. To be conducted at five sites in South Africa, Zimbabwe and the US. Expected start 2024.
2		**Dapivirine and levonorgestrel vaginal film**	**Univ of Pittsburgh** (USA)	**Vaginal film**	**Dapivirine** *NNRTI (ARV)* **Levonorgestrel** *(LNG) hormonal contraceptive*	**Women insert themselves**	**1 month**	As film slowly dissolves it would release both dapivirine and LNG until film completely dissolves	Pre-clinical
3		**Cabotegravir/ levonorgestrel hydrogel injectable**	**CONRAD** (USA)	**Injectable depot**	**Cabotegravir** *Integrase strand inhibitor (ARV)* **Levonorgestrel** (LNG) *hormonal contraceptive*	**Injection given under the skin**	**4-6 months**	Initially liquid, hydrogel forms into a small ball that would slowly release cabotegravir and LNG as it dissolves. (If needed, removable in first 1-2 months)	Pre-clinical
4		**Cabotegravir/ levonorgestrel dissolvable pellets**	**CONRAD** (USA)	**Pellet implant**	**Cabotegravir** *Integrase strand inhibitor (ARV)* **Levonorgestrel** (LNG) *hormonal contraceptive*	**Implanted under skin**	**Up to 1 year**	8-9+ tiny pellets with cabotegravir and 1 with LNG would be inserted; pellets slowly release active ingredients and dissolve over 9 months. over course of a year. (If needed, removable in first 1-2 months)	Pre-clinical

MATRIX Products and Planned Studies

Below are summaries of each of MATRIX's nine products, and where applicable, related studies. Products are grouped according to whether they contain existing active pharmaceutical ingredients (APIs) or novel APIs. Both groupings include dual-purpose products.

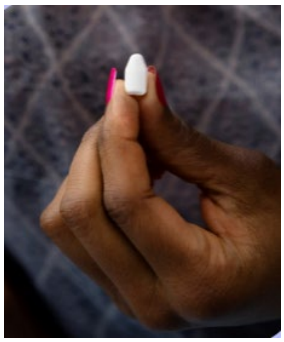
As previously noted, product and study summaries reflect their status at the time of the consultation (1 Sept 2023)

MATRIX Products with Existing Active Pharmaceutical Ingredients (APIs)

Seven of the nine products in the MATRIX portfolio contain an existing API (approved as HIV prevention in other formulations or for treatment), three of which are also dual-purpose products for the prevention of both HIV and unplanned pregnancy. Products with existing APIs are the TAF/EVG fast dissolving vaginal insert; the monthly dapivirine vaginal film and dual-purpose monthly dapivirine film; cabotegravir dissolvable pellets implant and cabotegravir injectable depot and dual-purpose versions of each of these products.

TAF/EVG Fast-Dissolving Vaginal Insert and the MATRIX-001 study

About the TAF/EVG Fast-Dissolving Vaginal Insert



The TAF/EVG fast-dissolving insert is an on-demand HIV prevention product that women would insert into their vagina around the time of sex. The insert, which resembles a bullet-shaped tablet, contains the antiretroviral (ARV) drugs tenofovir alafenamide (TAF) and elvitegravir (EVG). Once inside the vagina, the insert would begin to dissolve, and in doing so, release both TAF and EVG, which by mixing with vaginal fluid, get dispersed inside the vagina. Animal and laboratory studies suggest the insert would provide protection against HIV for up to three days.

The insert is the only female-controlled on-demand method in clinical trials. Such a method could appeal to women who don't want or are unable to use oral pre-exposure prophylaxis (PrEP), which requires taking an ARV tablet every day, or long-acting products like the monthly dapivirine vaginal ring or cabotegravir injections given every two months. It may be especially appealing to women who have infrequent or clustered sex and want only to use a product when needed, with local delivery (in the vagina) and like that it delivers drug locally, with little drug going elsewhere in the body.

The insert is being developed by CONRAD, a nonprofit research organization affiliated with Eastern Virginia Medical School in Norfolk, Va., USA, for its use both vaginally and rectally. The two active ingredients, TAF and EVG, are being provided by Gilead Sciences for CONRAD's development in the insert product.

TAF belongs to a class of ARVs called nucleoside reverse transcriptase inhibitors (NRTIs) that prevent HIV from making copies of itself inside human cells, therefore, preventing the spread of HIV inside the body. TAF has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of chronic hepatitis B and for the treatment and prevention of HIV in men who have sex with men when used in combination with another ARV drug called emtricitabine, or FTC. Laboratory and animal studies also indicate that TAF has activity against herpes simplex virus (HSV). The insert's second drug, EVG, has been approved by the U.S. FDA for the treatment of HIV in combination with other ARVs. EVG belongs to a different class of ARV drugs known as integrase inhibitors that block HIV from being able to integrate its genetic code into human cells – a step that occurs later in the HIV lifecycle.

Of the nine products being developed under MATRIX, the TAF/EVG fast-dissolving vaginal insert is the farthest along, having already been evaluated in placebo studies of the insert with no active drug and in first-in-human studies evaluating its safety and acceptability as a vaginal insert (CONRAD 146) and as a rectal insert (MTN-039). CONRAD-146, which was conducted among 16 women in the U.S., found single use as a vaginal insert safe and acceptable. Likewise, the MTN-039 study involving 23 participants found its single use as a rectal insert and two inserts used together posed no safety concerns. In both studies, results of laboratory tests of tissue and fluid samples showed drug levels compatible with protection against HIV.

MATRIX is evaluating the insert for its primary indication as a product to prevent HIV – and as a vaginal insert. Toward this end, it will be conducting MATRIX-001.

About the MATRIX-001 Study

In the MATRIX-001 Phase 1 study, researchers are evaluating the safety of the TAF/EVG vaginal insert when used multiple times over several days, as well as user acceptability and how and where the two drugs are taken up in the body. In addition, laboratory tests of participants' tissue samples will be conducted to assess its potential activity against both HIV and HSV. The study, which is the second Phase 1 trial of the TAF/EVG insert used vaginally and the first to enroll African women, will help determine whether the product should advance to Phase 2 studies to assess its safety and acceptability when used as designed, i.e., at or around the time of sex.

MATRIX-001 will enroll 60 women at three sites: the Kenya Medical Research Institute (KEMRI) Centre for Clinical Research Thika clinical research site (CRS),Centre for the AIDS Programme of Research in South Africa (CAPRISA) eThekwini CRS, in Durban; and Eastern Virginia Medical School (EVMS) in Norfolk, Va., USA. Participants will be randomly assigned to use either the TAF/EVG fast-dissolving insert or a placebo insert with no active drug. Each participant will use a total of 10 inserts – at first, every day for three consecutive days, and then every other day (every 48 hours) for two weeks. Participants will insert the products themselves, the first time being in the clinic, and with guidance from study staff. During the two to three months they are in the study, participants will undergo different tests and procedures and will be asked questions about product acceptability prior to, during and following insert use. The study is expected to take approximately one year to conduct, with results anticipated mid-2025.

Protocol co-chairs are Leila Mansoor, B.Pharm, PhD, from CAPRISA (South Africa) and Nelly Mugo, MBChB, MMed, MPH, from KEMRI (Kenya), both of whom also serve as the Investigator of Record (IoR) at their respective sites.

Monthly Dapivirine Vaginal Film, Dapivirine Dual-Purpose Film and MATRIX-002 study

About the Monthly Dapivirine Vaginal Film and Dapivirine Dual-Purpose Film

Similar to thin breath mint strips that dissolve in the mouth, vaginal films are products designed to dissolve after being inserted into the vagina. The use of films for HIV prevention has been explored in a number of studies conducted in the United States and several African countries, including acceptability studies of fast-dissolving films containing no active drug, finding that many women are both willing to and interested in using films to protect against HIV. Researchers have also conducted Phase 1 studies of films containing different ARVs as the active drug, including daily quick-dissolve films containing tenofovir or dapivirine, and a film containing an experimental ARV called MK-2048 designed to dissolve over the course of seven days. In each of these studies, the film was found to be safe, acceptable to use and to release drug as it dissolves within the desired timeframe.

The monthly dapivirine vaginal film is designed so that when placed inside the vagina and comes in contact with vaginal fluid, it slowly begins to dissolve, and in doing so, releases the ARV drug dapivirine. The drug continues to be slowly released over the course of a month until the film completely dissolves and all of the drug has been delivered in the vagina. This means there would be nothing to remove or discard before the user inserts a new film for another month of discreet protection.

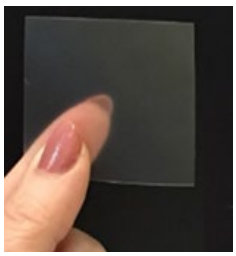
The monthly film is being developed by a team of researchers from the University of Pittsburgh and Magee-Womens Research Institute (MWRI). They are also developing a dual-purpose vaginal film for one month protection against both HIV and pregnancy, which, in addition to dapivirine, contains the hormonal contraceptive levonorgestrel (LNG). The University of Pittsburgh/MWRI team is collaborating with the Population Council, a global nonprofit research organization, which in 2022 acquired the dapivirine product pipeline from the International Partnership for Microbicides.

Dapivirine is already known to be safe and effective for preventing HIV when formulated as a monthly vaginal ring, which is approved in several African countries, including Kenya, South Africa and Zimbabwe. Like the dapivirine ring, the film is designed to deliver drug locally, within the vagina, with little drug going elsewhere in the body. Whereas the dapivirine ring contains 25 mg of active drug, 4-5 mg of which is released during the month it is worn, the vaginal film will contain about 35 mg of dapivirine, all of which would be released by the end of the month, once the film has completely dissolved. What impact this may have on safety and efficacy is yet to be established in clinical trials . The monthly dapivirine film has undergone extensive laboratory and animal (non-human primate) studies demonstrating that it is able to release drug over 30 days, and importantly, with no safety concerns. It has not yet been evaluated in women.

About the MATRIX-002 Study

Before evaluating the monthly dapivirine film for its safety, drug release and distribution in a first-in-human Phase 1 trial, researchers want to be sure that women – particularly women in Africa – are comfortable with the idea of using a vaginal film that takes one month to dissolve. The MATRIX-002 study of two prototypes of a monthly film containing no active drug will help answer this question. The study will also help determine the film design to be evaluated in subsequent trials of dapivirine film products, beginning with a monthly film containing dapivirine only, followed by the dapivirine and LNG dual-purpose film, which is earlier in its development.

MATRIX-002 will assess the acceptability, usability and safety of two prototype monthly vaginal films containing no active drug that are similar in size (2"x2") but differ in their shape – one has rounded corners, while the other has straight corners. As the first study of a vaginal film designed to dissolve over the course of a month, MATRIX-002 will be important for understanding how participants feel about using a monthly film, whether they are able to insert the films themselves with sufficient ease, which film is easier to insert, as well as what sexual partners think about the films. The study will also help to understand the kind of support and counseling women may need to use film and how best to address questions and concerns male partners may have.



MATRIX-002 will enroll 100 women and 30 sexual partners at five sites in four countries: In Kenya, at the KEMRI CRS; in South Africa, at the Aurum Institute Klerksdorp CRS and the Wits RHI CRS, Johannesburg; in Zimbabwe, at Harare Health and Research Consortium (HHRC) Zengeza CRS; and in the United States, at the University of Pittsburgh/MWRI CRS. Protocol chairs are Nyaradzo Mgodi, MBChB, MMed, from HHRC, who also serves as that site's IoR; and Alexandra Minnis, PhD, from RTI International, Berkeley, California.

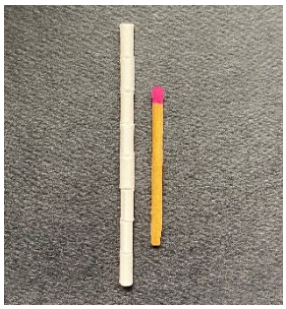
Women who enroll in the study will be randomly assigned to use one of the two placebo films. They will use their assigned film twice, for one month each. During the first month of film use, women are to refrain from vaginal sex and vaginal product use. During the second month, when a new film will be used, there will be no such restrictions. Women will insert the films themselves in the clinic with study staff providing guidance and instructions. As part of the study, participants will be asked questions about their experiences, including likes and dislikes, with film use, and up to 35 participants will also be asked to participate in an in-depth qualitative interview so that the study can gain deeper insight into women's experience with and views about the film. In-depth interviews will also be conducted with approximately 30 sexual partners. The study is anticipated to be completed in July or August 2024, with results expected by the end of the year (2024). A first-in-human study of the monthly dapivirine film is likely to be conducted in 2025.

Why design the study to evaluate two differently shaped films? If not for the feedback from stakeholder consultations convened in Kenya, South Africa, and Zimbabwe in 2022, during which prototype films were passed around, the MATRIX-002 study might have instead concentrated on the original square design. But upon learning that advocates and young women disliked the straight corners of the film, researchers rounded its corners, recognizing also that this modification would result in a slightly higher product cost. While cost is an important factor, so too are the preferences of women who will actually use the film, insight into which the MATRIX-002 study will provide.

Cabotegravir Dissolvable Pellets, Injectable Depot and Dual-Purpose Products

About the Cabotegravir Dissolvable Pellets and Dual-Purpose Pellets

The cabotegravir dissolvable pellets contain the ARV cabotegravir, which is already approved for both the treatment and prevention of HIV and/or under regulatory review for its potential approval in several countries. As HIV prevention, cabotegravir is highly effective against HIV when given as an intramuscular injection every two months, an approach familiarly referred to as CAB-LA.



Tiny pellets containing cabotegravir would be insert in a row just under the skin

The pellets implant would be administered by a healthcare provider using a hollow needle to insert 8-9 small pellets in a row, just under the skin (subcutaneously). Once placed under the skin, the pellets are designed to slowly dissolve and release drug for up to one year. Because the HIV drug is delivered throughout the body, there would be protection from all potential routes of HIV transmission. Furthermore, because the pellets would completely dissolve, there would be nothing to remove by a healthcare provider. If medically necessary, however,

removal may be possible within the first 1-2 months after insertion. Even after the pellets have completely dissolved, some drug may remain in the body for a period of time at levels that may no longer confer protection against HIV, thus, presenting a potential for risk of drug resistance should the user be exposed to HIV during that time. Laboratory and animal studies conducted by CONRAD thus far suggest that when cabotegravir is given subcutaneously rather than intramuscularly, as with CAB-LA., drug persists in the body for a shorter period of time.

The cabotegravir dissolvable pellets are being developed by CONRAD. CONRAD is also developing a dual-purpose pellets implant for protection against both HIV and unplanned pregnancy. In addition to the 8-9 pellets containing cabotegravir, the dual-purpose implant would also include a pellet containing LNG, a hormonal contraceptive.

Laboratory and animal research of both cabotegravir based pellets products are ongoing. Neither has been evaluated in humans.

About Cabotegravir Injectable Depot and Dual-Purpose Injectable Depot

Another cabotegravir-containing product being developed by CONRAD is cabotegravir injectable depot, as well as a dual-purpose injectable depot containing both cabotegravir and LNG. As with the pellets implants, both depot products are very early in their development.

With depot, cabotegravir is contained inside a liquid gel that a healthcare provider injects just under the skin (subcutaneously) using a small needle. After being injected, the hydrogel is designed to form into a small ball that, as it dissolves, slowly releases cabotegravir (or both cabotegravir and LNG) for up to 6 months. The small ball may be noticeable at first, but would get smaller and smaller, and eventually disappear after it is fully dissolved. Because it dissolves, there would be nothing to remove, similar to the pellets implant. Likewise, removal of the depot gel may be feasible within the first 1-2 months of injection if medically necessary.

Because drug resistance is a concern with use of CAB-LA, due to the length of time that drug remains in the body, researchers are mindful of this being a similar concern with any cabotegravir-containing products. As mentioned above, laboratory and animal studies conducted to date suggest drug resistance would be of less concern with the dissolvable pellets and injectable depot, mostly likely because with both methods, drug is delivered subcutaneously.

MATRIX Products with Novel APIs

Two of the nine products being developed through MATRIX contain novel APIs. Below are descriptions of the **Griffithsin Fast-Dissolving Vaginal Insert** and the **Non-ARV/Nonhormonal contraceptive Dual-Purpose Vaginal Ring.**

Griffithsin Fast-Dissolving Vaginal Insert

About the Griffithsin Fast-Dissolving Vaginal Insert

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 Griffithsin, a non-ARV protein originally discovered in algae but that researchers now produce in the laboratory. A woman would use her fingers to gently push the insert inside her vagina prior to sex. Once inside the vagina, the insert is designed to dissolve and mix with a woman's vaginal fluids to coat the inside of the vagina forming a barrier.

It would take less than 20 minutes for the insert to dissolve after being inserted. Initial studies suggest the insert would provide protection for 4-6 hours. Researchers have been seeking to extend the duration of protection to at least 12 hours. Studies involving non-human primates suggest this may be possible with inserts containing higher doses of Griffithsin.

Griffithsin binds to the outside of HIV and prevents its entry into healthy cells. Because the drug is non-ARV, and thus not used to treat HIV, researchers believe drug resistance is unlikely to be of concern should a woman be exposed to HIV while using the insert, though this would need to be evaluated in clinical studies. Animal and laboratory studies suggest the antiviral drug also has activity against other STIs (HSV and human papillovirus, or HPV). MATRIX is evaluating the product for its primary indication as a product for the prevention of HIV.

The insert would be a discreet product that women could carry in their purse or pocket; no applicator would be needed. Researchers anticipate it would be inexpensive, scalable and manufacturable in low- and middle-income countries.

Non-ARV/Nonhormonal Contraceptive Dual-Purpose Vaginal Ring and the MATRIX-003 Study

About the Non-ARV/Non-hormonal Contraceptive Dual-Purpose Vaginal Ring

The non-ARV/non-hormonal contraceptive dual-purpose vaginal ring is being developed by the Oak Crest Institute of Science as a method to protect women against both HIV and pregnancy for a month at a time. The ring, which is made of a soft and flexible silicone, is designed so that women would be able to easily insert and remove the ring themselves.

The ring has two compartments. One contains the anti-HIV agent, an antiviral peptide (protein fragment) that blocks viruses from attaching to, penetrating, and infecting healthy cells in the body. The other compartment contains a hormone-free contraceptive called a soluble Adenylate Cyclase (sAC) inhibitor that impedes the movement of sperm and its ability to penetrate and fertilize eggs.

When placed inside the vagina, the ring is designed to continuously release both drugs during the one month it is worn. Both agents act locally in the vaginal fluids. Animal and laboratory studies suggest the antiviral drug also has activity against HSV and human papillomavirus (HPV). MATRIX is supporting development of the vaginal ring for its primary indication to protect against HIV (and pregnancy).

Because the HIV drug is not an ARV, and hence, not used for the treatment of HIV, a woman would likely not develop ARV drug resistance should she be exposed to HIV while using the ring, though this will need to be confirmed in clinical trials.

Thus far, researchers have conducted one study involving 12 women in the US that evaluated short-term (one hour) use and ease of insertion and removal of placebo rings (containing no active drugs) that differed in design, geometry and hardness/stiffness. Women were instructed to perform various physical activities while the ring was in place, such coughing, squatting and jumping up and down. The study, which found no safety or usability concerns, guided the ring designs to be evaluated in the MATRIX-003 study, which will then determine the ring that would move forward into a first-in-human study of the vaginal ring containing the antiviral and non-hormonal contraceptive.

About the MATRIX-003 Study

While similarly sized vaginal rings have been found to be safe and acceptable with use over one-month or longer, the design of the Oak Crest dual-purpose ring, with its two cartridge-like compartments, is unlike other rings studied to date. As such, the MATRIX-003 is designed to collect data on the acceptability, usability and safety of two placebo rings (with neither of the active ingredients)and when used for a month at a time.

While the two placebo rings to be evaluated are similar in size and design, they have slight differences in flexibility and stiffness that may or may not impact user acceptability. The study will help determine whether there are differences between the two in terms of women's acceptability and ease of insertion and if (and how often) the ring comes out on its own. Importantly, experiences with use of the different vaginal rings in the context of sex will also be explored.

MATRIX-003 will enroll 100 HIV-negative women ages 18-45 and approximately 30 sexual partners at five sites: one in the United States (University of Pittsburgh/MWRI); three in South Africa (Aurum Institute, Wits RHI; CAPRISA – Vulindlela); and one in Zimbabwe (HHRC-Zengeza). Women in the study will use both placebo rings, each for approximately four weeks. Which placebo ring women use first will be determined by randomization. With each ring, women will be asked to abstain from sex for the first two weeks of use.

The study is expected to begin early 2024 and take approximately one year to conduct, with results early 2025. Protocol co-chairs are Kathryn Mngadi MBChB (Aurum Institute) and Krishnaveni (Surina) Reddy, MMedSci (Wits RHI). ■

Stakeholder Feedback and Discussion

Questions that were shared with stakeholders in advance of the consultation provided a framework for each feedback and discussion session. In the process, we also gained greater insight into the current and evolving context within which MATRIX activities are being conducted: Some questions were specific to the class of products, i.e., products containing existing active pharmaceutical ingredients (APIs) , products containing novel APIs and dual-purpose product; while other questions were overarching and relevant to all MATRIX products, its mission and overall approach. Comments and key take-aways regarding these questions are summarized below and grouped accordingly. Additional insights and recommendations are also included.

Takunda Sola (foreground), HIV Prevention and Key Populations Medical Officer with the Ministry of Health and Child Care in Zimbabwe, and Melissa Peet, Lead Scientist in Preclinical Development at CONRAD, listen intently to a presentation.

Overarching Questions

What is the best way for MATRIX product developers to engage with national medicines regulatory authorities or collaborative mechanisms now, i.e., early in the drug development process? Are there processes for early engagement?

Representatives from the South African Health Products Regulatory Authority (SAHPRA) and Medicines Control Authority of Zimbabwe (MRCZ) indicated that such processes existed and they would welcome the opportunity to engage directly with researchers and product developers. It could not be established if the same was true for Kenya, given that there was no one in attendance from the Pharmacy and Poisons Board.

> ***"We have provision for pre-submission meetings with product developers….. So as with SAHPRA, you just then request formally in writing, and possibly with a list of the questions where you need further clarity as the product developers and provide at least some information so that we can be clear on the products that you're working with, and how best we can assist you to facilitate the regulatory process."***
>
> **Rutendo Chaitezvi**
> **Senior Regulatory Officer, Pharmacovigilance and Clinical Trials Division**
> **Medicines Control Authority of Zimbabwe (MCAZ)**

Zazibona, the regional regulatory system for the Southern African Development Community (SADC), which includes Kenya, South Africa and Zimbabwe, does not have a formal process for early engagement, but it's quite likely that the African Medicines Agency (AMA) will have such a mechanism once it is fully operational, though it's not certain when this might be. That being said, it was mentioned that the African Vaccine Regulatory Forum (AVAREF) provided a mechanism for early engagement. AVAREF, which was established by the World Health Organization (WHO) is a network of African national regulatory authorities and ethics committees that conducts joint reviews of clinical trials and uses harmonization and reliance as pillars for capacity building. AVAREF's focus is no longer limited to vaccines;. Moreover, it also serves as a technical committee for the African Medicines Regulatory Harmonization (AMRH) initiative. The process is still quite new, especially for non-vaccine related research, and it also remained uncertain if and how the process would work with countries wanting to maintain some level of independent decision making, which stakeholders also saw as important. Even if MATRIX were to pursue regional mechanisms, it would still be prudent to engage at a country level as well.

"We have a continental platform that involves most of the regulators in Africa, which is AVAREF … they've recently established a scientific advice procedure, whereby you engage with them at an early stage of designing a trial, so that once a trial has been conducted, you have also buy-in from the regulator. And the good thing with a platform like AVAREF, … you get both the committee ethics review, as well as the protocol review and then you get a joint approval of a clinical trial.

But of course, the challenge remains with the decision making at a country level because you have a joint review, but then when it comes to countries, are these two processes connected? I think this is the question that the African Medicines Agency is going to then answer."

Alex Juma Ismail
Programme Officer, African Union Development Agency (AUDA-NEPAD), African Medicines Regulatory Harmonization (AMRH) initiative

"Individual countries still feel their responsibilities to the individual citizens."

Elizabeth Bukusi
Senior Principal Clinical Research Scientist, Kenya Medical Research Institute (KEMRI)
Chair, Bioethics Society of Kenya

While the question being asked was about early engagement with regulatory authorities, stakeholders recommended there be efforts to engage with ethics committees and Institutional Review Boards early in the process as well. In addition, MATRIX should endeavor to become familiar with each country's national HIV prevention plans and priorities and seek to engage with high-level policy makers (i.e., from Ministries of Health) to explain how MATRIX activities and products under development are or would be in alignment. Doing so would help ensure buy-in at the highest level and enable a smoother review process when the time comes.

Understanding the Changing Regulatory Environment in Africa: A Glossary of Terms

African Medicines Agency – established as a specialized agency of the African Union (AU) to enhance capacity for regulation of medical products in order to ensure access to quality, safe and effective products on the continent. Will coordinate and strengthen ongoing initiatives.

African Medicines Regulatory Harmonization (AMRH) initiative of AU's Development Agency (AUDA-NEPAD) that aims to harmonize regulatory policies and frameworks that are more effective, efficient and transparent

African Vaccine Regulatory Forum (AVAREF) – a network of African national regulatory authorities and ethics committees that conducts joint reviews of clinical trials and uses harmonization and reliance as pillars for capacity building. Founded by WHO, its focus is no longer just vaccines; serves as a technical committee for AMRH.

Harmonization – relating to the development of common technical requirements, standards, and guidelines for quality, safety, and efficacy in the regulation of pharmaceutical products.

Reliance – When a regulatory authority takes into account and gives significant weight to an evaluation by another regulator or trusted institution (e.g., WHO pre-qualification) in reaching its own independent decision

Regional Regulatory System – A collaborative registration process in which individual regulatory authorities operate under a common regulatory framework but not necessarily a common legal framework (e.g., Zazibona)

Zazibona – a regional regulatory system for the Southern African Development Community (SADC) originally established by Zambia, Zimbabwe, Botswana and Namibia. Decisions are recommendations only, and member states may still conduct its own review anyway.

▶ *MATRIX product developers plan to follow a development pathway defined by the US Food and Drug Administration– How can they keep in step with evolving regulatory processes (including reliance procedures) of African national medicines authorities and collaborative mechanisms? How should they fit into or adapt to the changing paradigm?*

Stakeholders made it quite clear that the US FDA as a primary pathway is no longer considered acceptable or ideal, especially for products intended mainly for African populations. The kind of studies the FDA may recommend product developers conduct may not be relevant to the African context, for example. But more importantly, following this pathway would make it more difficult to achieve what is ultimately being sought – a structure for and about the people of Africa and one that would leverage and enhance the capabilities of the African regulatory community.

"The FDA is set up to protect US citizens primarily. …. -This trickle down is no longer acceptable. What we're doing in the region… is trying to increase the maturity and the ability and the status of African regulators. And that's not going to work if the default is always back to the FDA, back to EMA. So, I would very, very strongly appeal to MATRIX as a structure that we find other innovative ways."

Helen Rees

Chair, South African Health Products Regulatory Authority (SAHPRA)

Having the FDA (or European Medicines Agency, EMA) as the primary regulatory pathway presents other challenges as well. Regardless of an FDA review's outcome, African regulatory authorities must still make their own determination in the best interests of the populations they serve, which cannot be done with confidence without having full access to data reports, which stakeholders said the FDA does not provide. Stakeholders were frustrated that the FDA's influence had become so far-reaching that it's being linked to funding mechanisms to support rollout of prevention products. For instance, countries cannot easily procure products through PEPFAR if the product has not undergone review or been approved by the FDA, even if the product would be of obvious benefit to the African population.

"You are mainly engaging with the US FDA and they hardly share the report unless you have a memorandum of understanding, and it also takes time. So, those are some of the things you need to consider if.you are intending to register your product in this region …. As much as we recognize the work done by FDA., as we do reliance, we still need the full data … we still need the full submission."

Mphako Ratlabyana

Manager, Pharmaceutical Evaluation and Management Pre-Registration Unit,
South African Health Products Regulatory Authority (SAHPRA)

"Part of the concern has always been that if it isn't FDA approved, then you may not be able to use US tax dollars for purchasing it. So that then becomes a bit of a benchmark that if you have it approved anywhere else, and the US FDA has not approved it, even if the product works, then the issue of scaling it up, getting it out, getting the product used becomes a challenge."

Elizabeth Bukusi

Senior Principal Clinical Research Scientist,
Kenya Medical Research Institute (KEMRI)
Chair, Bioethics Society of Kenya

Although the customary route for product developers would be a regulatory pathway defined by the FDA, stakeholders made an appeal to MATRIX that it still finds a way to work with the African Medicines Agency.

> ***"Now with the inception of the African Medicines Agency, the idea is to make sure that you have a continental regulatory body that at least … can get some level of respect."***
>
> **Alex Juma Ismail**
> **Programme Officer, African Union Development Agency (AUDA-NEPAD), Medicines Regulatory Harmonization (AMRH) initiative**

> ***"Looking at the presentations today, these look to me to be very complex products, not like a simple generic... So, you are still early in your trials. I think at some point when you finish, maybe consider also submitting through the AMA. I think we will be working on finalizing the continental process. And then we'll be running some pilot, then later on, I think the process of having full operational AMA will be in place and then it could also allow a bigger or quicker registration in countries if you went through that continental process."***
>
> **Mphako Ratlabyana**
> **Manager, Pharmaceutical Evaluation and Management Pre-Registration Unit, South African Health Products Regulatory Authority (SAHPRA)**

▶ *What should product developers be thinking about and doing now – at this early stage – to address potential concerns about costs of goods and delivery in sub-Saharan Africa? Are there considerations related to packaging or labeling?*

Products under development through MATRIX should align with national priorities and a case should be made for how this is so. Stakeholders emphasized that considerations regarding a product's potential cost and ease of delivery would be key and it would be wise to be thinking about the feasibility of products in these terms during their early development. Environmental considerations should also be made.

> ***"For us, the biggest challenge at the moment in introducing the new products is the availability, both in terms of cost… [and supply]. …. And I think those are the two things we need to look at: supply and cost. Especially with new products coming in… we need to make sure that the supply and the cost are negotiated upfront so that it actually assists us to make those products available …"***
>
> **Hasina Subedar**
> **Senior Technical Advisor, South Africa National Department of Health**

> ***"It's always quite important to take the national research agenda, the national health strategies and policies. This is where then the quality of the partnership you will have with the ministries will dictate how fast that research will go, and what benefits will come out of it for the country, the host country, as well as for the researchers themselves… …Which part of our development agenda is it answering to?"***
>
> **Tendai Kureya**
> **Executive Secretary, Medical Research Council of Zimbabwe**

Are there any lessons to be learned from reviews of the dapivirine vaginal ring and/or CAB-LA by national Essential Medicines List committees that can be applied to MATRIX products?

Similar themes emerged regarding the need to consider what gaps new products would fill as well as their acceptability to end-users and the health care providers who would be delivering these products. As such, there was appreciation for and interest in the work MATRIX is doing to understand the needs and preferences of potential end-users, healthcare providers and other key influencers. In terms of delivery, stakeholders talked about feasibility and cost being important considerations. It was also pointed that economic evaluations of products are part of the review process, with the salient metric being the product's affordability, or cost-efficiency, which should not be confused with cost-effectiveness. Whether a product will be affordable in terms of its impact on available resources is not the same as its cost-effectiveness, which is a product's added-value relative to its cost. As such, product developers should be careful not use the terms cost-efficiency and cost-effectiveness interchangeably when drawing conclusions about their products.

"What are the gaps that these products are going to address? The other critical element…make sure we also have a cost-benefit analysis, you know, which looks at the existing products we have, and how these new products are going to make a greater contribution. Because from an implementation point of view, and from a policy making point of view, we're not going to look at a product that's not going to add value, you know, and it's also in terms of looking at what is the cost of that value? And will we be able to afford it?"

Hasina Subedar

Senior Technical Advisor, South Africa National Department of Health

"Often people look at cost efficiency and say something's cost-effective. …but it's affordability, which is required, and they put those two words together, and say if it's cost-effective, it's affordable. And that's not actually true. And so part of the discussions around the modeling and the cost-efficiency model that is done, it must look at affordability ."

Marc Blockman

Former Chair, Essential Drugs Programme of South Africa
Chair, Health Sciences Human Research and Ethics Committee, University of Cape Town's Senate Ethics in Research Committee

"Our review process considers a whole series of things, moving from evidence, but also includes things like feasibility and acceptability … often what's lacking in our framework to make a decision is end-user acceptability, and also provider acceptability… These processes also include an economic evaluation component."

Renée de Waal
Co-chair, South African National Essential Medicines List Committee

ARVs versus Non-ARVs

What regulatory considerations are important to you and your approval procedures for products containing novel APIs, new chemical entities or new devices?

Reviews of non-ARV products weren't anticipated to be any different than reviews of ARV-based products. The same kind of data -- on safety and pharmacokinetics/pharmacodynamics, for example – would be required. But at the same time, stakeholders weren't able to provide a definitive answer to this question either (or to similar questions about dual-purpose products). It was during this session, however, that a recommendation was made that another meeting be convened to unpack what may or may not be required for these products. (see *Other Insights and Recommendations*.)

▶ *HIV drug resistance is not presumed to be of concern with products containing non-ARV agents, and therefore, it's also presumed that HIV testing would not be required. What is the likelihood and feasibility of product delivery without a requirement for HIV testing?*

While stakeholders expressed interest in the products containing novel agents, i.e., non-antiretroviral (non-ARV) drugs, they felt that the messaging about the potential benefits of these products needed to be tempered and more mindful of the realities. Just because the drugs are not used for the treatment of HIV, and therefore, drug resistance is not likely to occur should someone acquire HIV while using the product, doesn't mean HIV testing would not be required prior to and during use. HIV testing is to be a given in the delivery of any product, because testing is the best way to ensure access to treatment for someone who has acquired HIV. Whether the product contains ARVs or non-ARVs is not relevant.

> ***"From an HIV prevention perspective, we would still need to do HIV testing. The only question that would be there would be the frequency of the testing. Do we need to make it like, like every three months testing, or increase the period? I think those are the things that we would then need to think about when we have seen the efficacy of the product in the first place."***
>
> **Takunda Sola**
>
> **HIV Prevention and Key Populations Medical Officer, Ministry of Health and Child Care (Zimbabwe)**

> ***"Our conversation should be more person centered rather than product centered. And that would inform some of the decisions we are making, for example, do we have an idea of who we envision this product to be most attractive to? Can we characterize this end user? Because if we do that, it will inform part of the conversation we're having, for example, for HIV testing, does that necessarily have to be different from what you would do for the general population?."***
>
> **Murugi Michenii**
>
> **Head of Policy and Strategy**
> **National Syndemic Diseases Control Council (NSDCC) (Kenya)**

▶ *What are your views about the safety of non-ARV containing products versus ARV-based products?*

> ***"…a non-ARV based method, I think it will be welcomed by many people, in terms of our population, anything that is ARV based people have concerns. And we have to do quite a lot of education around the safety of using ARVs for HIV negative persons. But if you're promoting something that's not ARV based, I'm quite sure the acceptability will be much, much, much higher."***
>
> **Hasina Subedar**
>
> **Senior Technical Advisor, South Africa National Department of Health**

Dual-Purpose Products

- ***Are health care systems able to integrate combination products (HIV and contraception) into current primary health care programmes? If not, what is needed?***
  - ***Dual-prevention products may not be as effective as long-acting reversible contraceptives (LARCs) – should they be targeted to women who aren't already using contraception?***
  - ***What requirements will need to be fulfilled to include dual-purpose products into national policy and clinical guidelines?***
  - ***What might be the barriers and challenges with regard to delivery, availability and use of these products?***

Not all questions were addressed, but there was general agreement that health care burden would be a potential concern in the delivery of a dual-purpose products and needed to be addressed. There was also a sense of confidence that this could be done, given past experience.

> ***"So we have been able to show that it can be done and done well. But one of the biggest hurdles was the health care workers … we found what really helped was building clear training curricula that helped the health workers add this additional task in a meaningful way that provided them with efficiency, and then finding ways to motivate them to provide the care… how to ensure that they don't feel overloaded and that they feel skilled enough."***
>
> **Elizabeth Bukusi**
> **Senior Principal Clinical Research Scientist, KEMRI; Chair, Bioethics Society of Kenya**

> ***"In Zimbabwe, we have a good integration project, which we conducted in family planning clinics, where we started offering HIV testing services, STI screening services, PrEP, and self-testing HIV self-testing in in family planning clinics…, we've already demonstrated that integrating family planning services, contraception and HIV services, STI services is really good at working."***
>
> **Mkhokheli Ngwena**
> **National Professional Officer, The World Health Organization (Zimbabwe)**

- ***National regulators have yet to review applications for dual-purpose products – what should product developers be thinking about now that would help support potential approvals in the future?***
  - ***No FDA guidance has been issued surrounding a regulatory pathway for dual-purpose products. Are African national regulatory bodies and/or collaborative mechanisms aiming to define its own roadmap? What kind of discussions, if any, have taken place so far?***
  - ***Do you perceive any procedural barriers or challenges with respect to the review process of dual-purpose products?***
- ***How might MATRIX help facilitate or play a role in future discussions focused on regulatory considerations for dual-purpose products?***

Initially, the belief was that the review process would be no different for dual-purpose products, but that as with other product types, developers were welcome to engage with regulators early in the process for input on what kind of studies and data they would want to see. During the course of the discussion, it became more apparent that this was indeed unchartered territory, but also represented an opportunity for learning and capacity development. The focus of the conversation was now about what could or should be next steps, with one possibility being a meeting (s) with other key parties – perhaps even the FDA and WHO – to decide what kind of trials would be needed for the regulatory assessment of dual-purpose products.

"Given there are no guidance documents and policies available and it is a work in progress. I think it would be nice if you have representatives from the different regulatory bodies, across the different countries as well as representatives from the various stakeholders that you have represented here today to participate in the discussions purely because, as this becomes more of an area…where people are going to be conducting more trials, the regulatory body should also have some insight as to what they should be reviewing and … and what should we should be looking for in a protocol or in an application …all the key things, but from a dual-purpose product perspective."

Munira Khan

Member, University of KwaZulu-Natal Biomedical Research Ethics Committee (South Africa)

"This is very new. As you're saying, even the US FDA, I don't think they've come up with a guideline for trial design for this kind of product. So that's the only solution that I'm seeing would be to engage these regulators. I know one experience with a malaria vaccine. I think the USAID also engaged a number of regulators in the designing. So they had come up with three types of designs, and then they presented to this forum. And then after a number of discussions, then they came into an agreement of one of the designs. ….then it will be easy for you to go back to the regulator to say … these are the data that we've gotten from the studies, then it's easy to streamline the approvals process."

Alex Juma Ismail

Programme Officer, African Union Development Agency (AUDA-NEPAD), Medicines Regulatory Harmonization (AMRH) initiative

"Why don't we all sit and develop the guidance together, meaning FDA, WHO and ourselves and whoever else does not have the guidance? …. That's where you start before you even look at the product. I think that with a public health lens."

Precious Matsoso

Director, Health Regulatory Science Platform, Wits Health Consortium (South Africa)

Additional Insights and Recommendations

One of the things that came out of the discussion was support for MATRIX conducting early phase clinical trials in Africa, in addition to in the US, but also the need to be transparent and forthcoming in communications with community and participants that the potential benefits for participation in early phase trials is not what they would expect of a Phase 3 trial, i.e. post-trial access. Potential benefits at the individual level would be few. The benefit would be for future generations and the knowledge gained.

"I think the idea of having parallel studies both in the US and South Africa is a brilliant move. Historically, .., it's usually one or the other. And we all know that products have different impacts and outcomes and based on a number of variables within each community that you rolling out the study from an individual versus a community-level benefit. I think that from an ethical perspective, …. there is very little individual level benefit at this point. [Communities should be} a little more aware and accepting of the lack of individual level benefit for the greater benefit of generations to come.".

Munira Khan

Member, University of KwaZulu-Natal Biomedical Research Ethics Committee (South Africa)

"I think for early phase studies, the critical ethical concept we're asking people to understand is the risk-to-knowledge ratio, that the risks to participants in these early phase studies need to be sufficiently mitigated and offset by social value. "

Cathy Slack

Consultant to CASPR (Coalition to Accelerate and Support Prevention Research)
Honorary Research Fellow , University of KwaZulu-Natal School of Law ,

One of the more concrete suggestions to come out of the meeting was that the African Union Development Agency (AUDA-NEPAD), the seat of the AMRH, convene a meeting with all relevant parties – including regional bodies and national authorities – to help define the way forward. The questions being asked of stakeholders were specific to MATRIX products, but had relevance beyond MATRIX, especially within the context of a new and emerging regulatory structure in Africa. It was further suggested that USAID, through MATRIX, might be able to provide financial support for such a meeting. ■

Left to right: Edward Serem, Head of the Division of Reproductive and Maternal Health Services, Ministry of Health, Kenya; Mkhokheli Ngwena, National Professional Officer, The World Health Organization (Zimbabwe), with Clariator Mvurume, Senior Regulatory Officer in the Evaluations and Registration Division at the Medicines Control Authority of Zimbabwe; Dominicah Thosago, Medical Registration , South African Health Product Regulatory Authority

Summary and Considerations

A critical takeaway from the 1 Sept 2023 Regulatory and Product Development Consultation is that significant strides have been made in strengthening the capacity of African regulatory bodies and that it also remains a work in progress. Collaborative mechanisms, harmonization and reliance have been the pillars for building capacity of national regulatory authorities and related structures and in the establishment of an independent continental regulatory decision-making body for and about the African people. A movement is also now afoot to see that product development and manufacturing can take place on the African continent, recognizing that an investment in local infrastructure would cost considerably less than importing medicines and technology. The sense of pride in what has been accomplished so far was in full display during the meeting. So, too, was stakeholders' steadfast determination to overcome what remaining obstacles may stand in the way of realizing regulatory autonomy and independence in Africa.

Rutendo Chaitezvi, Senior Regulatory Officer in the Pharmacovigilance and Clinical Trials Division at the Medicines Control Authority of Zimbabwe (MCAZ)

MATRIX's mission and objectives are in keeping with and supportive of the paradigm shift taking place in Africa. MATRIX aims to expedite the research and development of a range of HIV prevention products for women that go beyond being safe and effective. Indeed, MATRIX's goal is to support the research and development of products that are also acceptable, affordable, scalable and deliverable in the settings where they are needed most. Through its North-South Partnerships, MATRIX also aims to strengthen the research and development capacity of African investigators in order to facilitate full and sustainable ownership of this work into the future.

For MATRIX, the consultation provided important insight but also demonstrated that it has much to learn and to better understand about the new and emerging regulatory structures.

Likewise, many of the questions MATRIX asked of stakeholders served only to raise new ones. This is to be expected, given that it's a time of transition. Regulatory processes and bodies are still evolving or have not yet been clearly defined or instituted. There were questions on issues only now beginning to come to the forefront, including what kind of regulatory guidance there should be for the development of dual-purpose products.

Clearly, more discussion will be required. One of the more concrete suggestions to come out of the meeting was that the African Union Development Agency (AUDA-NEPAD), the seat of the African Medicines Regulatory Harmonization (AMRH) initiative, convene a meeting with all relevant parties – including regional bodies and national authorities – to help outline processes for current and future MATRIX products. Such a meeting, which it was suggested MATRIX sponsor, would help provide more clarity for how MATRIX product developers should be working with the African Medicines Authority (AMA) and national regulatory authorities, both now and as these structures mature – a discussion of great relevance to other research organizations and product developers as well. Indeed, stakeholders were strong in their belief that the US Food and Drug Administration (FDA) as a primary regulatory pathway was no longer acceptable – certainly not for products of the like being developed under MATRIX, which are intended primarily for use by African women. MATRIX is not positioned to address the concerns stakeholders mentioned having with the FDA but is hopeful that stakeholders' voices will be heard and result in reforms being made. But, are there any solutions in the meantime? Should product developers pursue parallel pathways?

While much of the discussion was about new structures, such as the AMA and the African Vaccine Regulatory Forum (AVAREF), stakeholders cautioned that even if MATRIX and its product developers were to follow regional pathways, in-country engagement would still be essential.

Specific recommendations that came out of the consultation, some of which have also been mentioned above, were to:

- Work with/support AUDA-NEPAD in convening a follow-up meeting to unpack unanswered questions and chart the way forward regarding processes for MATRIX products. (As noted by stakeholders, such a meeting would be an important opportunity for regional capacity building, harmonization and learning.)
- Convene/help spearhead a meeting focused on regulatory guidance and trial design considerations for dual-purpose products. (Again, stakeholders felt such a meeting would provide for capacity building and learning.)

- Seek a regulatory pathway that includes the AMA, either in parallel with the FDA or in some collaborative manner.
- Take advantage of mechanisms for early engagement with national regulatory authorities (i.e., the South African Health Products Regulatory Authority, or SAHPRA; and the Medicines Control Authority of Zimbabwe, or MCAZ) and determine whether similar mechanisms exist for Kenya's Pharmacy and Poisons Control Board.
- Consider submitting study protocols to AVAREF to enable joint reviews by relevant national regulatory and ethics committees.
- Develop strategies for in-country stakeholder engagement that align with national priorities and plans and include high-level representatives within Ministries of Health and other decision-making bodies.
- Consider early engagement with ethics committees/Institutional Review Boards regarding the design and conduct of early phase clinical trials
- Temper messaging about the potential benefits of products, in particular products containing non-ARVs – for example it cannot be said that HIV testing would not be required with use of these products, as this is not the current reality.

Other considerations:

- Stakeholders are eager for any opportunity for capacity building and learning, and indicated particular interest in such learnings around early research and development. While many of the recommendations listed above can be considered capacity building activities, are there other ways MATRIX can contribute to the establishment and operational success of these new structures on the continent?
- Given the importance that stakeholders placed on end-user and healthcare provider acceptability research, MATRIX should seek ways for sharing findings from activities of the Design to Delivery activity hub.

The consultation has provided MATRIX with much to think about. It has also made clear that there is still much more to talk about. MATRIX intends to follow-up with all attendees, and with some stakeholders individually as well, with any relevant updates and to discuss proposed next steps. Of note, MATRIX is planning to hold its next face-to-face stakeholder meeting in Nairobi (late August/early September 2024). Special effort will be made to engage with representatives from Kenya's Pharmacy and Poisons Control Board, who were not in attendance at the last consultation, and to ensure their participation in larger and future discussion as well.

Engagement with stakeholders this early in the research process is not typically done. MATRIX is unique in that respect. Sharon Hillier, executive director of MATRIX, acknowledged this in her introduction, as well as the fact that there were no guarantees the products being developed under MATRIX would succeed anyway – such are the realities of early research and development. The fact that MATRIX was seeking stakeholder feedback at this early juncture she called "an experiment in early drug development," telling stakeholders that that they were part of that experiment.

It was a message that was taken to heart by at least one stakeholder, as reflected in the following statement made at the end of the day. ■

"I just want to reflect a bit on what Sharon said. When this meeting started, she said this is an experiment. … What I see here is that we do not have an end-to-end platform where we do research and development from the beginning in this continent, research and development from the beginning, from bench to bedside, or from bench to people's arms. Yes, [we do] clinical trials, but if this [MATRIX] is an experiment to help us do R&D, and to do it all the way as a continent. I think this is a good experiment."

Precious Matsoso

Director, Health Regulatory Science Platform, Wits Health Consortium (South Africa)

Annex 1: Consultation Agenda

Regulatory and Product Development Stakeholders Consultation

Johannesburg, South Africa

1 September 2023 – Southern Sun Rosebank Hotel

Welcome dinner and reception 31 August 2023 for All Stakeholder Meeting Attendees

08:00-08:30		**Registration**
08:30-09:15	**Session 1**	**Welcome and Introductions** • ***Sharon Hillier*** (Magee-Womens Research Institute - MWRI) • ***Thesla Palanee Phillips*** (Wits Reproductive Health and HIV Institute – Wits RHI) • ***MATRIX In-country Investigators***
Context and Setting the Stage		
09:15 -9:25	**Session 2**	**The Current HIV Prevention Landscape and the Need for More Options** • ***Nyaradzo Mgodi*** (Harare Health Research Consortium - HHRC)
9:25-10:05	**Session 3**	**MATRIX: Developing the next generation of HIV prevention products for women** • ***Sharon Hillier*** (MWRI) • ***Thesla Palanee Phillips*** (Wits RHI)
10:05-10:20		**Tea Break**
MATRIX Products with existing Active Pharmaceutical Ingredients (APIs)		
10:20-10:55	**Session 4**	**TAF/EVG Fast-Dissolving Vaginal Insert *and* MATRIX-001** • ***Melissa Peet*** (CONRAD) • ***Leila Mansoor*** (Centre for the AIDS Programme of Research in South Africa - CAPRISA) **Questions and Discussion:** ***Thesla Palanee-Phillips*** (Wits RHI) – Moderator
10:55-11:30	**Session 5**	**Dapivirine Vaginal Film, Dapivirine Dual-Purpose Film *and* MATRIX-002** • ***Lisa Rohan*** (University of Pittsburgh) • ***Nyaradzo Mgodi*** (HHRC) **Questions and Discussion:** ***Thesla Palanee-Phillips*** (Wits RHI) – Moderator
11:30 -12:05	**Session 6**	**Cabotegravir Dissolvable Pellets, Injectable Depot and Dual-Purpose Products** • ***Gustavo Doncel*** (CONRAD) **Questions and Discussion:** ***Thesla Palanee-Phillips*** (Wits RHI) – Moderator
12:05-12:50	**Session 7**	**Stakeholder Feedback and Discussion: *MATRIX Products with Existing APIs*** ***Sharon Hillier*** (MWRI), ***Thesla Palanee-Phillips*** (Wits RHI) - Moderators • *What is the best way for MATRIX product developers to engage with national medicines regulatory authorities or collaborative mechanisms now, i.e., early in the drug development process? Are there processes for early engagement?* • *MATRIX product developers plan to follow a development pathway defined by the US Food and Drug Development. How can they keep in step with evolving regulatory processes (including reliance procedures) of African national medicines authorities and collaborative mechanisms? How should they fit into/adapt to the changing paradigm?* • *Are there any lessons to be learned from reviews of the dapivirine vaginal ring and/or CAB-LA by national Essential Medicines List committees that can be applied to MATRIX products?* • *What should product developers be thinking about and doing now – at this early stage – to address potential concerns about costs of goods and delivery in sub-Saharan Africa? Are there considerations related to packaging or labeling?*

12:50-1:50		**Lunch**
		MATRIX Products with Novel Active Pharmaceutical Ingredients (APIs)
13:50-14:15	**Session 8**	**Griffithsin Fast-Dissolving Vaginal Insert** • ***Lisa Haddad*** (Population Council) **Questions and Discussion:** ***Kenneth Ngure*** (JKUAT) – Moderator
14:15-14:50	**Session 9**	**Non-ARV/Nonhormonal Contraceptive Dual-Purpose Vaginal Ring *and* MATRIX-003** • ***John Moss*** (Oak Crest Institute of Science) • ***Kathryn Mngadi*** (The Aurum Institute) **Questions and Discussion:** ***Kenneth Ngure*** (JKUAT) – Moderator
14:50-15:15	**Session 10**	**Stakeholder Feedback and Discussion: *MATRIX Products with Novel APIs*** ***Sharon Hillier*** (MWRI), ***Thesla Palanee-Phillips*** (Wits RHI) - Moderators • *What regulatory considerations are important to you and your approval procedures for products containing novel APIs, new chemical entities (NCEs) or new devices?* • *HIV drug resistance is not presumed to be of concern with products containing non-ARV agents, and therefore, it's also presumed that HIV testing would not be required. What is the likelihood and feasibility of product delivery without a requirement for HIV testing?* • *What are your views about the safety of non-ARV containing products versus ARV-based prevention?* • *Do you have any recommendation for how we could communicate these products to you earlier and the approaches we plan to use to design clinical trials to test them?*
15:15-15:30		**Tea Break**
		MATRIX Dual-Purpose Products

15:30-16:45	**Session 11**	**Stakeholder Feedback and Discussion: *MATRIX Dual-Purpose Products***
		Sharon Hillier (MWRI), ***Thesla Palanee-Phillips*** (Wits RHI) - Moderators
		• *Are health care systems able to integrate combination products (HIV and contraception) into current primary health care programmes? If not, what is needed?*
		  ○ *Dual-prevention products may not be as effective as LARCs – should they be targeted to women who aren't already using contraception?*
		  ○ *What requirements will need to be fulfilled to include dual-purpose products into national policy and clinical guidelines?*
		  ○ *What might be the barriers and challenges with regard to their delivery, availability and use?*
		• *National regulators have yet to review applications for dual-purpose products – what should product developers be thinking about now that would help support potential approvals in the future?*
		  ○ *No FDA guidance has been issued surrounding a regulatory pathway for dual-purpose products. Are African national regulatory bodies and/or collaborative mechanisms aiming to define its own roadmap? What kind of discussions, if any, have taken place so far?*
		  ○ *Do you perceive any procedural barriers or challenges with respect to the review process of dual-purpose products?*
		  ○ *How might MATRIX help facilitate or play a role in future discussions focused on regulatory considerations for dual-purpose products?*

		Summary and Next Steps
16:45-17:30	**Session 12**	**Summary and Next Steps** ***Thesla Palanee-Phillips*** (Wits RHI) - Moderator
17:30- 19:30		**Informal Reception**

Annex 2: Meeting Participants and Speakers Bios

Regulatory and Product Development Stakeholders Consultation

Johannesburg, South Africa
1 September 2023 – Southern Sun Rosebank Hotel

Meeting Participants

STAKEHOLDERS

Peter Arimi

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Dr. Peter Arimi has more than 20 years of experience in international epidemiological research and public health spanning Eastern Africa, Southern Africa, the United States and the Pacific. He is currently Program Director of the HIV Prevention Technical Support Unit (HIV TSU) of Partners for Health and Development in Africa (PHDA), a health system strengthening partnership of PHDA with the National AIDS and STI Control Programme (NASCOP) and National Syndemic Diseases Control Council (NSDCC) that aims to strengthen the effectiveness of the HIV response in Kenya. The HIV TSU, which is funded by the Bill and Melinda Gates Foundation through the University of Manitoba, is embedded within NSDCC and NASCOP. As Program Director, Dr. Arimi provides overall technical and management oversight of the project. He's previously served as Senior Regional Health Specialist, United States Agency for International Development, providing oversight of USAID's East Africa regional health program; Clinical Director, Clinton Health Access Initiative, Papua New Guinea; Clinical Research Coordinating Physician, Harvard School of Public Health, Botswana; Senior Medical Officer, Ministry of Health, Botswana; and Medical Officer, Ministry of Health, Kenya.

Marc Blockman

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Marc Blockman is professor in the Department of Internal Medicine and senior consultant in the division of clinical pharmacology at Groote Schuur Hospital and the University of Cape Town. He has been involved in the science of clinical pharmacology and its application to clinical medicine for 35 years. He believes strongly in evidence-based medicine. He has been involved since 1995 with the Essential Drugs Programme of South Africa, including as chair. He is Chair of the Health Sciences Human Research and Ethics Committee, the University of Cape Town's Senate Ethics in Research Committee; as well as various data safety monitoring boards. Recognised as an expert on international, national and provincial drug policy, he is chair of the South African Health Products Regulatory Authority (SAHPRA) pharmacovigilance expert committee and a member of SAHPRA's clinical expert committee. He is an International Consultant for the WHO and executive member of the Provincial Government of the Western Cape's Pharmacy and Therapeutics Advisory Committee.

Tiwadayo Braimoh

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Tiwadayo Braimoh has over 20 years of work experience improving access to medicines and in health policy and health systems strengthening. He currently works with Medicines Patent Pool (MPP), Geneva, Switzerland where he leads globally on the policy aspects of access to COVID-19 medicines and medical countermeasures to pandemics through intellectual property licensing and technology transfer and as the focal point person for MPP across diseases areas for Africa. He started off his career in the pharmaceutical industry as a medical representative, became a product manager and then a Business Development Manager. After nearly a decade, he left the private sector to join Clinton Health Access Initiative (CHAI) where he worked on public health programs to improve access to medicines and with governments on access, health systems and health financing policies and programs. He holds an MSc in Health Policy, Planning and Financing from London School of Economics and London School of Hygiene and Tropical Medicine and an MBA from the University of Lagos. He is also a Pharmacist and Fellow of the West African Postgraduate College of Pharmacists.

Elizabeth Bukusi

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Elizabeth Anne Bukusi (ObGyn), MPH, PhD, PGD (Research Ethics), Masters in Bioethics, is a certified IRB Professional. She is a Senior Principal Clinical Research Scientist at the Kenya Medical Research Institute (KEMRI), a Research Professor at the University of Washington (Departments of Obstetrics and Gynecology and Global health), an honorary lecturer at Aga Khan University in Nairobi and Maseno University (Department of Obstetrics and Gynecology) and Volunteer Clinical faculty – Professor at the University of California San Francisco (Department of Obstetrics, Gynecology & Reproductive Sciences).In addition to her substantial experience in conducting socio-behavioral and biomedical research and providing HIV care, mentoring and training, she has a strong interest in research and clinical ethics and the development of systems and structures for regulation of research at KEMRI and nationally. She is the chairperson of the National Bioethics Society of Kenya, (BSK), a multidisciplinary, non-political, non-discriminatory, and not-for-profit organization aiming to for high ethical standards in bio-medical research, medicine and health care in Kenya. She Chaired the WHO HRP Alliance (capacity building for RH research) 2016 to 2021, and is a trustee for the HIV Trust, and an Elected Fellow of the African Academy of Sciences.

Rutendo Chaitezvi

Email: rchaitezvi@mcaz.co.zw

Rutendo Chaitezvi is a Senior Regulatory Officer in the Pharmacovigilance and Clinical Trials (PVCT) Division at the Medicines Control Authority of Zimbabwe (MCAZ) with five years of experience in regulatory affairs with a focus on clinical trials and medicines vigilance. She has experience in clinical trial application evaluation, processing amendments to clinical trials, conducting GCP inspections, and medicines and vaccines vigilance activities. She has participated as a speaker in a clinical trials oversight regulatory systems strengthening training of fellow African medicines regulatory authorities in 2021. She is part of the team responsible for publishing the MCAZ Medicines Information Bulletin. She holds a Bachelor of Pharmacy Degree from the Harare Institute of Technology and is currently pursuing a Master of Science in Pharmaceutical Biotechnology degree at the Chinhoyi University of Technology.

Benson Chikati

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Benson Chikati is Acting Executive Director at the Zimbabwe National Family Planning Council (ZNFPC), a role he has assumed in January 2022. From 2016-2021, he was Director of Administration and Finance at ZNFPC, responsible for overseeing administrative and human resources management functions, and between 2005 and 2016, was Head of the Human Resources Unit. He began his career at the University of Zimbabwe as a Senior Administration Assistant and Assistant Registrar. Throughout his career, Mr. Chikati has had the privilege of collaborating with numerous national and international organizations involved in family planning, sexual reproductive health, HIV and AIDS, and human resources development. He has played pivotal roles in formulating human resource policy and promoting human resources development in the fields of Public Health, Population and Sustainable Development, and Population and Policy Analysis through facilitation of scholarship programs with sponsoring and training institutions. He holds a Master's Degree in Public Administration from the University of Zimbabwe.

Karen Cohen

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Karen Cohen, MBChB, MMed (Clin Pharm) MSc(Epidemiology), is associate professor in the Division of Clinical Pharmacology, Department of Medicine, at the University of Cape Town. She has extensive experience in the supporting rational medicine selection and the essential medicines programme and has contributed to development of treatment guidelines at facility level, regionally, nationally and internationally. Professor Cohen is a member of South Africa's National Essential Medicines List Committee (NEMLC), a structure mandated by the Minister of Health to select essential medicines for use in South Africa at primary, secondary and tertiary levels of care. She chairs the Primary Healthcare and Adult Hospital Level Expert Review Committee of NEMLC, which makes recommendations to the NEMLC based on reviewing available evidence.

Reneé de Waal

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Reneé de Waal is the co-chair of the South African National Essential Medicines List Committee, which is tasked with advising the government regarding the selection of medicines for use in public sector health facilities and developing standard treatment guidelines for a wide range of priority health conditions. She has been involved in technical expert review sub-committees for the Essential Drugs Programme since 2011 and has been a co-editor of the South African Medicines Formulary since 2009. Reneé is a medical doctor with a Master of Public Health (Heath Economics) degree, and a Diploma in Pharmaceutical Medicine (UK). She has a background in clinical pharmacology, and currently works as a researcher at the Center for Infectious Disease Epidemiology and Research, School of Public Health, University of Cape Town.

Joey Gouws

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From 2017 until her retirement in 2023, Joey Gouws was Team Lead of Inspections for the World Health Organisation (WHO) Prequalification Programme, based in Geneva, Switzerland, responsible for the oversight of all inspections relating to medicines, vaccines, medical devices and vector control products. Prior to joining the WHO, she was Registrar of Medicines for the Medicines Control Council (MCC) of South Africa from 2015-2017. Among her positions during her 15 years with the Department of Health, South Africa, was Head of the medicines inspectorate, which she was appointed to in 2002. As a pharmacist, her experience includes retail pharmacy, hospital pharmacy and managing regulatory affairs for the pharmaceutical company Bayer (PTY) LTD, Johannesburg. Dr. Gouws holds Science and Pharmacy bachelors degrees and a Master's and PhD in Pharmaceuticals from the University of Potchefstroom, South Africa, as well as an MBA from the University of Pretoria, South Africa.

Alex Juma Ismail

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Mr. Alex Juma Ismail is a Programme Officer at African Union Development Agency (AUDA-NEPAD, working under the Medicines Regulatory Harmonization (AMRH) initiative, specializing in regulatory systems strengthening and harmonization. He is focused on supporting the operationalization of the African Medicines Agency (AMA), particularly in the formation and strengthening of continental technical committees that lead medical products regulatory activities in Africa. Mr. Ismail has more than eight years of experience in the medical and pharmaceutical industries. He is a pharmacist by training and has previously worked for both private pharmaceutical companies and governmental regulatory bodies In East and Southern Africa. He was also actively engaged in the regional economic communities' medicines regulatory harmonization programmes for the East African Community and the Southern African Development Community (SADC).

Munira Khan

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Munira Khan has vast experience in clinical research, including as a research clinician, and principal investigator; and serves as a member of the University of KwaZulu-Natal Biomedical Research Ethics Committee. Currently, Dr. Khan is Head of Research and Clinical Trials for THINK (Tuberculosis and HIV Investigative Network), a non-profit organisation founded in 2013 to improve the quality of life of people affected by TB and HIV in South Africa and around the world. As a research and health impact organisation, THINK works with international research institutions, the pharmaceutical industry and global health partners including the Global Fund, United States Agency for International Development (USAID) and Doctors Without Borders.

Tendai Kureya

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Professor Tendayi Kureya is the Executive Secretary of the Medical Research Council of Zimbabwe (MRCZ). He was appointed to the MRCZ board by The Minister of Health in 2017. His background is in Biostatistics, Business Administration and Sustainable Development. He has over 25 years' experience in research, data analysis, organisational development, and policy review. Professor Kureya has previously worked in the NGO sector, focusing on advocacy and development research. Between 2004 and 2012, Kureya was the programme representative for Irish Aid in Zimbabwe. He assisted in establishing the Expanded Support Programme which later became the Health Development Fund in Zimbabwe. In 2004, Professor Kureya established Development Data, a consultancy that provides cutting edge research and data management services in Southern Africa.

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Regina Maithufi is Deputy Director, HIV Prevention Strategies, South Africa National Department of Health (NDoH). Previously, she served as Technical Advisor, HIV Prevention, NDoH; as Senior Technical Officer for the Futures Group, and TB/HIV Expansion Project Manager at the University Research Cooperation in Pretoria, South Africa.

Rumbidzai Manyevere

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Rumbidzai Manyevere is a regulatory officer in the Pharmacovigilance and Clinical Trials (PVCT) division of the Medicines Control Authority of Zimbabwe (MCAZ) since 2018. She has five (5) years' experience in medicine regulation specifically evaluation of clinical trial applications, protocol amendments plus other clinical trial-related documents and GCP inspections; and medicines & vaccines vigilance activities. She has participated as a speaker in a clinical trials oversight regulatory systems strengthening training of fellow African medicines regulatory authorities in 2021. She contributes to pharmacovigilance systems strengthening initiatives in Zimbabwe which include conducting regular pharmacovigilance trainings, and assisting in writing and publishing the MCAZ Medicines Information Bulletin. She was a co author of the recently published manuscript titled, "Descriptive Research Study of the Adverse Events Following Immunization (AEFIs) Surveillance System in Zimbabwe." She holds a Bachelor of Pharmacy Honours degrees from the University of Zimbabwe.

Jerimia Manyika

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Jeremia is Social Worker cum Demographer currently serving as the Advisor for Equality and Rights in UNAIDS Zimbabwe Country Office. He graduated with a BSW Hons (Bachelor of Social Work Honours Degree from the University of Zimbabwe in 2006, acquired a Master of Science in Demography and Population studies (MDPS) from the Great Zimbabwe University in 2016. He has extensive experience in generating strategic guidelines based on community generated evidence and has produced numerous HIV response strategic documents SOPs and Implementation plans currently in use in Zimbabwe. Jeremia has worked in various portfolios in the government of Zimbabwe and civil society organisations with communities in socio economic development, gender, social justice, migration and child protection. He has worked for the National AIDS Council as a National Coordinator responsible for Key Populations Programing in Zimbabwe. His work experience in HIV response spans over 13 years working with youth, women and girls, Key Populations among them sex workers, MSM, Trans and prison inmates. He is a serving member of the African Health and HIV Prevention Partnership Network (AHHPPN) advocating for good prison health in Africa and various other technical working groups for HIV response in Zimbabwe.

Precious Matsoso

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Precious Matsoso is Director of the Health Regulatory Science Platform, a division of the Wits Health Consortium, and an Honorary Lecturer in the Department of Pharmacy and Pharmacology, University of the Witwatersrand, Johannesburg, South Africa. She is also Co-Chair of the World Health Organization (WHO)'s Intergovernmental Negotiating Body to Draft and Negotiate a WHO Convention, agreement or other international instrument on pandemic prevention, preparedness, and response (INB). Recently appointed Adjunct Professor at the University of Sunway, she was the Chair of the Independent Oversight and Advisory Committee of the WHO Emergency Programme. She was previously Director-General of the National Department of Health of South Africa and Registrar for South Africa's Medicines Control Council and also served as Director of Public Health Innovation and Intellectual Property and Director of Technical Cooperation for Essential Medicines and Traditional Medicines at WHO and as member and Chair of the WHO Executive Board.

Murugi Micheni

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Dr. Murugi Micheni is the Head of Policy and Strategy at the National Syndemic Diseases Control Council (NSDCC) in Kenya. She is a Research Physician and Clinical Epidemiologist with expertise in HIV and TB biomedical and socio-behavioral research, and care. Her areas of interest are in the development and implementation of research protocols and programs examining HIV risk and its reduction, and of the socio-cultural influencers of effective care and health promotion, particularly among populations at increased HIV risk and vulnerability.

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Orapeleng Motlhaoleng is public health practitioner with a vast experience in the public health space. He has held positions in clinical research and health systems strengthening. He's currently with the National Department of Health as a Deputy Director responsible for both PrEP and PEP implementation. He holds a Master of Public Health degree, and currently a PhD candidate in the same discipline.

Shungu Munyati

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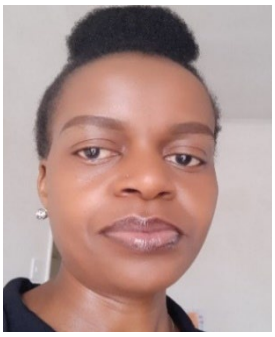
Dr. Shungu Munyati is Director-General of the Biomedical Research & Training Institute (BRTI) from May 2017, having been Assistant Director-General since 2007. BRTI, an independent, not-for-profit research and training institution, provides a strong platform for inter-collaborative and interdisciplinary local and international funded research, focusing on public health, HIV; TB, Malaria, COVID19, NCDs, laboratory systems and implementation science. From 1997-2006, she was Deputy Director, National Institute of Health Research (formerly Blair Research Institute), within the Ministry of Health and from 2016-2019 the Chairperson of the Medical Research Council of Zimbabwe (MRCZ), a statutory body responsible for research oversight, coordination and promotion of research and also serves the national research ethics committee. Dr Munyati has administered fellowships and coordinated training grants for HIV/AIDS and TB research to support postgraduate training. Her passion is to contribute towards building a critical mass of young African research scientists who can contribute to health development through research. She has a wealth of experience as a medical researcher and research administrator .Other areas of interest include water, sanitation, diarrheal disease transmission, socio-behavioral research on HIV/AIDS, OVC programmes and health systems research. She holds a BSc (Hons) Applied Biology, from North East London Polytechnic, UK; an MSc (Double major) Immunology/Microbiology, from Cornell University, USA, and a PhD from the College of Health Sciences, University of Zimbabwe, where she studied the association between HIV, smoking and respiratory illness.



Clariator Mvurume

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Clariator Mvurume is a Senior Regulatory Officer in the Evaluations and Registration Division at the Medicines Control Authority of Zimbabwe (MCAZ). She is a team lead for human allopathic medicines with more than 8 years' experience in medicines regulation. She is the country's representative at the Zazibona forum for assessors and a rapporteur of the Regulatory Capacity Development - Technical Committee. Having studied Pharmacy at the University of Zimbabwe, she went on to study for a Master of Science in Pharmaceutical Biotechnology at the Chinhoyi University of Technology. Recently she graduated from Purdue University, USA, with a Master of Science in Biotechnology Innovation and Regulatory Science. Since 2021 she has been a Global Health Protection Programme fellow for clinical assessments.

Violet Naanyu

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Violet Naanyu, PhD, MA, MA, MSc, is Associate Professor of Sociology at Moi University; Visiting Scholar, Aga Khan University; and Graduate Faculty Scholar & Member of the Graduate Faculty of Northern Illinois University, USA (2020-2024). She is Field Co-Director for the Academic Model Providing Access to Healthcare (AMPATH) Research Network – a collaboration of investigators from over 15 institutions in North America and Kenya, and Founder and Director, Qualitative Research Core, AMPATH Program. She is Co-Founder & Board Member, Fountain Projects and Research Office, Kenya; and a Board Member, International Centre for Reproductive Health. She serves as a member of the National Scientific and Ethics Committee, National Commission for Science, Technology & Innovations, Kenya; Committee Member, Bioethics Society of Kenya; and Member on two institutional research and ethics committees in Kenya. Her interests are in global bioethics and evaluations designed to improve research and healthcare in resource-limited settings.

Mkhokheli Ngwenya

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Mkhokheli Ngwenya is a Medical Doctor by profession and holds a Master in Public Health. He has over 18 years of experience in the clinical and/or programmatic management of TB and HIV in various roles in government and international health agencies. He sits in various technical working groups and committees for TB and HIV in Zimbabwe. Mkhokheli has experience in programme reviews and development of national strategic plans, technical guidelines, and training material. He also has experience in planning and managing donor projects. Mkhokheli has been involved in various research activities in TB and HIV including population-based surveys and operations research in Zimbabwe. He brings a wealth of knowledge in TB/HIV programming and research in Zimbabwe. He is currently working for WHO Zimbabwe country office as a National Professional Officer.

Patricia Oluoch

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Rose Patricia Oluoch, PhD, is a Public Health Specialist with over 20 years' experience in combination HIV prevention programming, currently as Program Management Specialist at the US Agency for International Development/Kenya as the team leader of the HIV Prevention and Social Service and previously with the Centers for Disease Control (CDC) Kenya. Her expertise is in program design implementation and monitoring, and the strategic, technical, organizational, and financial oversight of HIV prevention programs, including PrEP, gender-based violence, HIV testing services, programming for key and vulnerable populations, OVC, adolescent girls and young women and voluntary male medical circumcision and monitoring of implementing partners' cooperative agreements implementation. She is the technical lead in PrEP implementation for the PEPFAR program in Kenya and led in the roll out of PrEP in public health facilities and for adolescent girls and young women through the PEPFAR DREAMS program. She has expertise conducting and monitoring studies and was the technical lead for the last violence against children study (VACS) in Kenya, among others, and has published in peer reviewed journals. Dr. Oluoch was editor of Kenya's first guidelines for prevention of mother to child transmission (PMTCT) services. She has worked with government in development of several HIV policy and implementation guidelines and is recipient of the Presidential Award of the Moran of the Burning Spear.

Lillian Omutoko

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Dr. Lillian Omutoko is an Educationist and Bioethicist. She holds a PhD in Education, a Master's Degree in Global Bioethics, a Postgraduate Diploma in Health Research Ethics and a Certificate in Responsible Conduct in International Research. Lillian is a Senior Lecturer at University of Nairobi, Department of Educational Management, Policy and Curriculum Studies. Dr. Omutoko is a recipient of Fogarty Awards from National Institutes of Health for a fellowship at University of Washington and Stellenbosch University where she studied Health Research Ethics. She is involved in establishment of Hospital Ethics Committees in Kenya. She has attended several workshops and conferences in Bioethics nationally and internationally. She is a member of the National Scientific Ethics Research Committee, Kenyatta National Hospital-University of Nairobi Ethics Research Committee; Bioethics Society of Kenya; Research Ethics Association of Southern Africa and Africa Bioethics Consortium. Lillian is a fellow of the University Administrative Support Program- Research Management and Leadership Program sponsored by Carnegie New York Corporation. Her current passion is Research Compliance.

Mopo Radebe

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Mopo Radebe is currently Associate Director of HIV Prevention at the Clinton Health Access Initiative. She holds a PhD Degree from the University of KwaZulu-Natal, with a specialty in Virology. Before joining CHAI, Mopo served as the Technical Lead for HIV Prevention at the World Health Organization in South Africa and the WHO Regional PrEP Specialist supporting PrEP implementation in the sub-Saharan region. Mopo has extensive experience providing technical support to Ministries of Health in the sub-Saharan region, including HIV program planning and design, development of implementation guidance and tools/aids, program implementation, and monitoring and evaluation. Prior to her work in public health, Mopo was a research Scientist working on HIV vaccine design, with a special focus on understanding of how virus-host interactions lead to immune-mediated mechanisms of HIV control. Mopo has co-authored several peer-reviewed articles and book chapters on HIV and adolescent health. She has also presented research papers in several international conferences.

Mphako Ratlabyana

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Mr. Mphako Brighton Ratlabyana is currently the manager in the Pharmaceutical Evaluation and Management Pre-Registration Unit within the South African Health Products Regulatory Authority (SAHPRA). Prior to assuming management responsibilities, he worked as a Medicines Registration Officer, responsible for evaluating both pharmaceutical quality (CMC) and Bioequivalence aspects. He holds a Bachelor of Pharmacy degree (BPHARM) from University of Limpopo and M.Sc. Pharmacy administration and Policy regulation from University of the Western Cape. Prior to joining SAHPRA, he worked as a pharmacist in retail, private hospital, and public sector hospitals. He possesses extensive knowledge in the field of medicines regulation both locally and internationally. Mphako is very passionate about access to quality, safe, efficacious and affordable medicines and participates in various international and regional platforms. He is the focal person for Zazibona (SADC) collaborative registration procedure, alternate member of Continental EMP-TC, member of ministerial pricing committee and Co-chair of International Pharmaceutical Regulators Programme Quality working group (IPRP QWG). He also serves under various SAHPRA committees such as Policy committee, Priority Request Review Committee and Registration committee. His research interest is in transparency in medicines registration decision making process as well as implementation of reliance mechanisms in medicines registration.

Helen Rees

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Professor Helen Rees is Founder and Executive Director of Wits RHI, the largest research Institute at Wits University. Helen is an internationally recognised health practitioner who has dedicated her professional career to improving global health with a focus on public health in Africa. A Personal Professor in Wits' Department of Obstetrics and Gynaecology and Co-Founder/Co-Director of ALIVE (African Leadership in Vaccinology Expertise), Wits University's flagship vaccinology programme. she is an Honorary Professor in the Department of Clinical Research at the London School of Hygiene and Tropical Medicine and a Fellow at Cambridge University's Murray Edwards College. She is chair of the South African Health Products Regulatory Authority, and a member of South Africa's National Advisory Group on Immunization and of the Scientific Advisory Committee of the South African National Institute of Communicable Diseases. She is Chair of the WHO's African Regional Immunisation Technical Advisory Group and of the Emergency Committee on Polio and Co-Chair of WHO's Working Group on Ebola vaccines. Helen has authored or co-authored more than 250 academic publications, given more than 400 invited plenary and keynote addresses, and chaired numerous national and international meetings.

Paul Ruff

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Professor Paul Ruff was Chief Specialist, Professor and Head of the Division of Medical Oncology at the University of Witwatersrand Faculty of Health Sciences and Charlotte Maxeke Johannesburg Academic Hospital from October 2002 until December 2021. He is now Emeritus Professor in the School of Clinical Medicine, at the University of Witwatersrand, Faculty of Heath Sciences. He is Principal Investigator of the SA Medical Research Council / University of Witwatersrand Common Epithelial Cancer Research Centre since 2015. Professor Ruff has been Chair of the South African Health Products Regulatory Authority Clinical Trials Committee since 2015 and was Vice-Chair of the Ministerial Advisory Committee on Cancer Control and Prevention until the end of 2021. He is the incoming Chair of the Wits Human Research Ethics Committee (Wits HREC) He is a Member of National Essential Medicines List Committee from 2017 and was Chair of the Tertiary/Quaternary Essential Medicines List Committee from 2017-2021. Prof Ruff has authored or co-authored over 150 scientific papers, predominantly in the field of colorectal cancer, in various peer-reviewed journals including the New England Journal of Medicine, Journal of Clinical Oncology and Lancet Oncology, as well as presenting over 250 papers and posters at local and international scientific meetings.

Sithembile Ruzariro

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Sithembile is a Principal Research Compliance Officer at the Medical Research Council of Zimbabwe (MCAZ) Research Compliance Unit. The MRCZ houses the National Ethics Committee that is responsible for reviewing and approving all health research in Zimbabwe, including Clinical Trials. Sithembile coordinates the activities of the National Ethics Committee and ensures compliance of the health research enterprise with all related regulatory policies and guidelines. A Bioethicist, who has an MSc in bioethics, Sithembile's research interests include ethical, legal and social issues in biobanking, policy issues related to human research participants, consent issues and involvement of vulnerable groups in research. She has conducted research on the research governance system in order to improve the quality of research especially when using cutting edge technology, while protecting human participants.

Edward K Serem

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Dr Edward Serem is an obstetrician gynaecologist and Head of the Division of Reproductive and Maternal Health Services, Ministry of Health, Kenya. Dr Serem has the overall responsibility of periodic National review of policies, guidelines, standard operating procedures, protocols, data analysis, research and technical assistance and building the capacity of health care workers at the sub-national level on reproductive health service

Levi Singh

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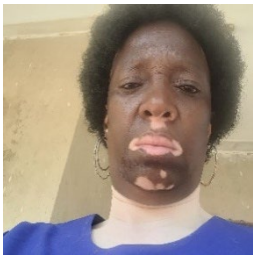
Levi Singh works with the SRHR Africa Trust as regional youth and policy officer. As former secretary general of the African youth and adolescent network on population and development (AfriYAN), he now serves as a mentor to the current executive committee of the network. Levi works extensively on systems for the meaningful engagement, participation, and leadership of young people in health policy making spaces using data to influence policy dialogue through civic diplomacy. Levi's professional work and advocacy experience include the Africa agenda 2063, UN Sustainable development goals, African health strategy, ICPD Plan of Action and Universal health coverage with a focus on adolescent & youth health and well-being. Levi serves as a founding member of the United Nations global partnership forum on comprehensive sexuality education and as a SADC regional youth parliamentarian to the 3rd SADC youth parliamentary forum. He is currently pursuing my studies further in politics, philosophy, and economics.



Caroline Sirewu

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Caroline Sirewu is a registered nurse with midwifery and public health nursing qualification who is also qualified with a Master of Science in Nursing and a Master of Non-Profit Organization. She has been working for the National AIDS Council as a National Coordinator in the Treatment and Care & Support area for 15 years. Working with a team of stakeholders, she provides reviewing and updating of Technical Guidelines in the following thematic areas: PMTCT, HTS, STI, PrEP, ART, TB & HIV, Nutrition & HIV and Community Care. The work in the thematic area has also included work in the PrEP area. She has coordinated Community based Programmes in two Non-Governmental Organizations namely Africare International, Zimbabwe Office in an HIV programming and World Vision International, Zimbabwe Office in a Mother to Child Programme. Her experience working in the community started over 20 years ago in the Ministry of Health and Child Care (MOHCC) where she worked for 10 years. In addition in the MOHCC, she has also worked with general patients and in the midwifery area.

Cathy Slack

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Catherine M Slack (PhD) is a clinical psychologist and consultant to CASPR (Coalition to Accelerate and Support Prevention Research) funded by the United States. Agency for International Development (USAID) as well as an Honorary Research Fellow at the School of Law, University of KwaZulu-Natal. She has over 20 years of experience in research, tool development and training around ethics complexities in HIV prevention trials. She was a member of the National Health Research Ethics Council in South Africa for 9 years – a body that sets norms and standards for research ethics. Catherine is especially interested in how empirical data might contribute to normative recommendations.

Takunda Sola

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Takunda Sola is a Public Health Practitioner with over 10 years of experience in both the public sector and the NGO workspace. He currently serves as the HIV Prevention and Key Populations Medical Officer with the Ministry of Health and Child Care (MoHCC) in Zimbabwe. He is responsible for supporting the HIV Prevention Department in introducing new HIV prevention interventions to the public sector market, health worker capacity building, ensuring quality standards in Key Populations programming in the public sector, among other responsibilities.

Hasina Subedar

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Hasina Subedar is a Senior Technical Advisor, National Department of Health, South Africa, a role she has served since 2010. She has played a leading role in introducing and expanding the use of oral HIV Pre-Exposure Prophylaxis (PrEP) in South Africa and is currently involved in supporting the introduction of new biomedical and long-acting HIV prevention products. She was involved in the national roll-out of the Human Papillomavirus (HPV) vaccination 2013-2015, has contributed to the revitalization of Primary Health Care (PHC) services in South Africa, which is essential for ensuring accessible and quality healthcare services for all citizens This involved integration of Community Health Workers into the public health system to reach underserved populations and providing essential healthcare service and; establishment of Ward-Based Outreach Teams as an extension of PHC clinics to strengthen and improve access to healthcare services at a community level.

Dominicah Thosago

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Dominicah Thosago is a Medical Registration Officer Grade 111 (MRO) at South African Health Product Regulatory Authority (SAHPRA), a position she's held since 2012. Previously, she was a practicing pharmacist in both retail and hospital for 9 years. As MRO for SAHPRA, she is experienced in clinical trials regulation. During her tenure, her unit has reduced the timelines for clinical trial approvals by more 80 percent, with clinical trial applications being finalized within 80 working days from receipt, and developed guidelines for clinical trials that are published on the SAHPRA website. She is a registered pharmacist and holds a B Pharm degree from the University of Limpopo.

Nonhlanhla Zwangobani

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Dr. Nonhlanhla Zwangobani, a holder of the Bachelor of Medicine and Surgery Degrees and master's degree in Public Health has experience in HIV, Sexual Reproductive Health and Rights and COVID-19. She served as a Technical Director for the Zimbabwe National Family Planning Council, mandated to coordinate SRHR programming in the country; worked as a COVID-19 epidemiologist with the World Health Organisation, and currently she leads CHAI's HIV prevention work in the Zimbabwe country office.

MATRIX – SPEAKERS and MODERATORS

Gustavo Doncel

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Gustavo Doncel is Scientific and Executive Director of CONRAD, a U.S.-based biomedical R&D organization focused on developing innovative user-centered affordable technologies aimed at improving global health, particularly in the areas of HIV/STI prevention, contraception/Family Planning, and Reproductive Health. He is also a tenured Professor of Obstetrics and Gynecology and Microbiology and Molecular Cell Biology at Eastern Virginia Medical School (EVMS). He holds both MD and PhD degrees and is a translational scientist with more than 35 years of experience. He has authored more than 180 scientific publications in the areas of contraception, HIV/STI prevention, fertility, sperm biology, pharmacokinetics and reproductive immunology. He is/has been a reviewer for the National Institutes of Health (NIH), the World Health Organization, the European Community (EC), and Bill and Melinda Gates Foundation. He serves as a scientific advisor for various research projects and organizations focused on biomedical prevention efforts and drug development. Among other awards, he received the Science Team Award from the Association for Clinical and Translational Science. Dr. Doncel is principal investigator of ongoing multi-center research projects on women's health issues and product development related to contraception, HIV/STI prevention and reproductive and maternal health, including a project on long-acting HIV prevention under MATRIX.

Lisa Haddad

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Lisa Haddad Medical Director of the Center for Biomedical Research at the Population Council, leading clinical development efforts to advance the Center's sexual and reproductive health product portfolio, including novel contraceptives and multi-purpose prevention technologies. She came to the Population Council from the Obstetrics & Gynecology Department, Emory University School of Medicine, where her research focused on reproductive health in high-risk populations, specifically among women living with and at risk for HIV. Her research has helped bring a clearer understanding of the interplay of sex hormones on the reproductive immune system and is helping to inform care and prevention approaches for women at high risk of HIV infection who also need safe and effective contraception. She has served as a principal investigator or co-investigator on several research projects funded by the US National Institutes of Health. including the Women's Interagency HIV Study, a longitudinal study to understand the natural history and impact of HIV on women in the US; and the CHIME study, a prospective cohort aimed at elucidating the interplay of both endogenous and exogenous sex hormones and the vaginal microbiome on the reproductive immune system. Dr. Haddad received an MD from the State University of New York, Stony Brook, an MS from New York University, an MPH from the Emory University Rollins School of Public Health.

Sharon Hillier

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Sharon Hillier, Ph.D., is the Richard Sweet Professor of Reproductive Infectious Disease and Vice-Chair for Faculty Affairs, University of Pittsburgh School of Medicine, Department of Obstetrics, Gynecology and Reproductive Sciences, with joint appointments in the departments of Microbiology and Molecular Genetics. She is also a senior scientist at the Magee-Womens Research Institute, where she serves as Executive Director of the United States Agency for International Development (USAID)-funded MATRIX collaborative, which is focused on the development of innovative HIV prevention and dual-purpose products for women. A recognized leader in HIV biomedical prevention, Dr. Hillier has more than 30 years' experience leading microbicide research, including as principal investigator of the National Institutes of Health-funded Microbicide Trials Network. Under Dr. Hillier's leadership, the MTN conducted more than 43 studies, including first-in-human trials of vaginal and rectal microbicides; among the first HIV prevention studies involving pregnant and breastfeeding women; and a suite of studies that contributed to regulatory approval of the monthly dapivirine vaginal ring. A specialist in reproductive infectious diseases and a self-described vaginal ecologist, her laboratory research focuses on understanding the vaginal microbiome.

Leila Mansoor

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Leila Mansoor, BPharm, PhD, is Senior Scientist at the Centre for the AIDS Programme of Research in South Africa (CAPRISA), University of KwaZulu-Natal. For MATRIX, she is the Co-Lead of Social Behavioral Research in Clinical Trials, a Pillar within the Design to Delivery Hub, protocol co-chair.of the MATRIX-001 Phase 1 study of the TAF/EVG fast-dissolving vaginal insert and site investigator for the MATRIX-003 acceptability and safety study of two placebo prototype monthly vaginal rings. She has more than 15 years of extensive clinical trial experience with pivotal research in evaluating HIV prevention biotechnologies for young women including development and implementation of novel approaches to adherence support particularly for low literacy level and research naïve populations. Her research interests include HIV prevention clinical research, adherence support and measures in clinical trials, as well as social science research focusing on patient's knowledge about, attitudes toward and perceptions of their medicine and disease state.

Nyaradzo Mgodi

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Nyaradzo Mgodi, MBCHB, MMED, is a clinical pathologist with 15 years' experience conducting clinical trials assessing topical microbicides, intravaginal rings, oral/injectable products for HIV PrEP among adolescents, heterosexual women, MSM and transgender people. She was protocol co-Chair for the proof-of-concept Antibody Mediated Prevention (AMP) studies among people at risk for HIV, Clinical Research Site Leader and Investigator of Record for numerous Microbicide Trials Network (MTN) studies conducted at the University of Zimbabwe Clinical Trials Research Centre (UZ-CTRC), including MTN-025/HOPE, the open-label follow-on study of the monthly dapivirine vaginal ring, for which she also served as protocol co-chair. Dr. Mgodi is co-lead of the Clinical Trials Hub under MATRIX, principal investigator of the Harare Health and Research Consortium and protocol co-chair of the MATRIX-002 acceptability and safety study of two prototype placebo monthly vaginal films . Dr. Mgodi is scientific reviewer and board member at the Medical Research Council of Zimbabwe. She was Zimbabwe Population-based HIV Impact Assessment - ZIMPHIA's technical adviser and is a Portfolio Management Advisory Committee member for CONRAD'S Project NIX HIV assessing next-generation products for prevention of HIV in women.

Kathryn Mngadi

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Dr Kathryn Mngadi (MBChB, Dip HIV Man SA, MPhil Pall Med, Dip Epi, MSc Clin Trials) is a South African investigator working mainly in HIV, TB and COVID prevention research over 25 years. She qualified at the Nelson Mandela School of Medicine (1987) and worked in clinical medicine before joining Anglogold Health Services in South Africa, under the guidance of The Aurum Institute. As principal investigator for Aurum Kleksdorp, she has worked mostly with adolescent girls and young women, especially on the VOICE study, and continued this with CAPRISA 008 in 2011. She rejoined The Aurum Institute in 2011 as Clinical Research Site leader, site PI and protocol co-chair for the HVTN 107 and HVTN 705 / Imbokodo studies. She serves on several committees, including trial steering and safety committees, Data Safety and Monitoring Boards and is a review and section editor for the Frontiers Reproductive Health Journal (HIV and STIs), and the African Journal of Public Health, respectively. She is very proud to be a co-chair for the MATRIX-003 study.

John Moss

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John A. Moss, Ph.D. holds the position of Senior Faculty at the Oak Crest Institute of Science, an independent, non-profit research and education center in Monrovia, California. He earned a B.S. in chemistry at Davidson College (Davidson, NC) and a Ph.D. in inorganic chemistry from the University of North Carolina at Chapel Hill. Following a post-doctoral fellowship at California Institute of Technology (Caltech), he joined Oak Crest in 2001. For more than 15 years, a primary focus of his research has been sustained-release drug delivery for HIV prevention. Dr. Moss has a diverse range of research and development interests including: long-acting biomedical technology and strategies for prevention and treatment of infectious disease, application and development of advanced biomedical imaging methods, biomedical and spectroscopic instrument development, materials and materials processing for biomedical applications, and early-stage medical device manufacturing.

Kenneth Ngure

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Kenneth Ngure, MPH, PGDSTI/HIV, MSC, PhD, is s an Associate Professor and the Chair Department of Community Health, College of Health Sciences, and Dean f the School of Public Health at Jomo Kenyatta University of Agriculture and Technology (JKUAT), Kenya. He is also an Affiliate Associate Professor of the Department of Global Health, University of Washington, Seattle, USA. He is also a behavioral scientist affiliated with the Microbicide Trials Network (MTN), the HIV Prevention Trials Network (HPTN) and International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network Ngure is also a biomedical HIV prevention expert having been an investigator in several landmark studies including Partners PrEP trial, Partners (PrEP) Demonstration Project, Partners Scale-UP Project, REACH (MTN 034) and is currently involved in projects to simplify PrEP delivery, and under MATRIX, is Co-Lead of End-User Product Preferences Research, a Pillar within the Design to Delivery Hub. He is a member of the PrEP Technical Working Group of the Ministry of Health, Kenya.

Melissa Peet

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M. Melissa Peet is a Lead Scientist in Preclinical Development at CONRAD, a nonprofit biomedical R&D organization nested within Eastern Virginia Medical School (EVMS) with a social mission to improve global health for women through the development of innovative, user-centered technologies targeted for contraception, HIV/STI prevention and reproductive and maternal health. Dr. Peet holds a PhD degree in behavioral pharmacology and has gained close to 20 years of combined experience as a Study Director at a contract research organization (CRO) and as a preclinical scientist at CONRAD. As a Study Director, she conducted over 250 studies evaluating medical devices, combination products, small molecules, biologics, and vaccines. Her primary focus has been on evaluating and assessing the safety, pharmacokinetics, and efficacy of novel products targeted to women's health using various animal models for advancement to clinical trials.

Thesla Palanee-Phillips

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Thesla Palanee-Phillips, M Med Sci, PhD, MSc, is the Director of Clinical Trials at the Wits Reproductive Health and HIV Institute (Wits RHI) in Johannesburg, South Africa, and Deputy Director of MATRIX, a USAID-funded program that aims to expedite the research and development of HIV prevention products for women – including products designed to protect against both HIV and pregnancy. She holds a joint appointment at the University of the Witwatersrand as an Associate Professor in the Faculty of Health Sciences and an Affiliate Associate Professor of epidemiology at the University of Washington School of Public Health. Trained as a medical laboratory scientist, she has expanded her expertise to include clinical trials design and implementation and integration of complex laboratory components as well as qualitative, behavioral, and implementation science-framed questions into clinical trials and investigator-driven research. She has particular interest in research that bridges HIV prevention with sexual/reproductive health, issues impacting adherence to HIV prevention interventions in the context of sexual violence and studies of interventions related to mitigation of risk of HIV. Dr. Palanee-Philips served as protocol chair of the ASPIRE (MTN-020) Phase III trial of the monthly dapivirine vaginal ring as well as the HOPE (MTN-025) open-label follow-on study of the ring.

Lisa Rohan

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Lisa Rohan is a Professor of Pharmaceutical Sciences in the School of Pharmacy, and Professor of Obstetrics, Gynecology & Reproductive Sciences in the School of Medicine, both at the University of Pittsburgh, and an investigator at the University of Pittsburgh-affiliated Magee-Womens Research Institute (MWRI). Her laboratory research, which is based at MWRI, is focused in the design, development and assessment of drug delivery systems for STIs and HIV prevention, gynecological oncology and other women's health applications. Prior to her academic career, Dr. Rohan was employed in the pharmaceutical industry. Her experience there covered all aspects of product development, including pre-formulation, formulation development and assessment, scale up, and clinical studies. She has been working in the area of product development for women's health issues for the past 17 years. Dr. Rohan obtained a Bachelor of Science in Chemical Engineering from West Virginia University and a Ph.D. in Pharmaceutics from the University of Pittsburgh School of Pharmacy. After completion of her Ph.D. work, Dr. Rohan completed a Postdoctoral Fellowship in the Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Pittsburgh School of medicine, focused on mucosal immunology.

MATRIX – PARTNERS and COLLABORATORS

Shannon Allen

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Dr. Shannon Allen is a Health Science Specialist within the Research Division of the Office of HIV and AIDS at the United States Agency for International Development (USAID). Shannon is the technical lead for one of the largest Microbicide programs, MATRIX (**M**icrobicide R&D to **A**dvance HIV Prevention **T**echnologies through **R**esponsive **I**nnovation and e**X**cellence), ever awarded which is designed to accelerate research and development of innovative biomedical HIV prevention technologies that women can use to protect themselves. Prior to this role, she was a Senior Technical Advisor for development of long-acting HIV products at USAID. Before that, she served as an HIV/AIDS Public Health Prevention Advisor at the Office of the Global AIDS Coordinator and Health Diplomacy where she assumed an intermediary role building bridges between hard core biomedical research and HIV prevention public health programs. Shannon is also a trained Virologist and obtained her PhD in Cell and Molecular Biology from Northwestern University and holds other degrees including a Masters in Applied Molecular Physiology and a Bachelors in PreMed/Biology.

Sher Shah Amin

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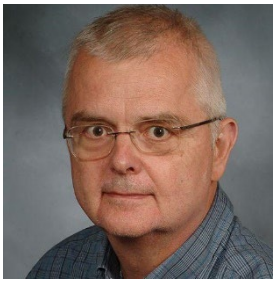
Sher Shah Amin, MD, MPH, is supporting the MATRIX project as a Lead Grants Specialist at Magee-Womens Research Institute. Sher Shah is a public health professional with over 15 years of experience in managing and implementing various health programs and projects at national and global levels. Prior to joining MWRI, Sher Shah has been working with the U.S. Agency for International Development, international non-governmental organizations and Afghanistan Ministry of Public Health. In his 6 years tenure with USAID, he has been managing USAID's two nationally implemented health projects as an AOR and Activity Manager focusing on maternal and child health in Afghanistan.



Jochen Buck

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Jochen Buck, MD, PhD., is Professor in Pharmacology at Weill Cornell Medicine, the Medical College of Cornell University, in New York, New York. Jochen co-directs a laboratory with his colleague and friend Prof. Lonny Levin that is studying how sperm is activated. Earlier this year, they published results of pre-clinical studies in Nature Communications demonstrating that an on-demand male contraceptive is possible through a mechanism that temporarily stops sperm in their tracks and prevents pregnancies. Jochen is collaborating with the Oak Crest Institute of Science in the development of an intra vaginal ring for the prevention of both HIV and unintended pregnancy.

Gabriela Gomez

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Gabriela Gomez is an infectious disease epidemiologist with over 15 years' experience supporting R&D and introduction pathways for new prevention and therapeutic technologies in low- and middle-income countries. After receiving her PhD at Imperial College London, she went on to work at the Amsterdam Institute for Global Health and Development (AIGHD) and the London School of Hygiene and Tropical Medicine (LSHTM). She co-led a BMGF-funded demonstration project for the introduction of pre-exposure prophylaxis for HIV in South Africa and led an implementation project to expand the cross-country provision of antiretroviral treatment for truck drivers in Zambia, Zimbabwe, and South Africa. Her academic research has focused on the integration of economic theory into infectious disease modelling to advance R&D and policy in TB and HIV prevention. She spent three years in industry as a Decision Science Expert for Sanofi, where she co-chaired of the Health Economic, Operational Research and Medical Scientific Review Committee and oversaw modelling activities to support the equitable allocation across markets of key products during the COVID pandemic and for financial valuations of pandemic preparedness investments. She currently works at IAVI as Senior Director Global Access and is an honorary associate professor at LSHTM. Gabriela is Co-Lead of MATRIX's Business, Market Dynamics and Commercialization Hub (BACH).

Bethany Young Holt

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Bethany Young Holt, PhD., MPH**.,** is Project Director, Public Health Institute based in Oakland California, and Co-Lead of MATRIX's Business, Market Dynamics and Commercialization Hub (BACH). She brings over 25 years of experience in sexual and reproductive health, including HIV prevention. An epidemiologist by training, Bethany founded CAMI Health, and subsequently co-founded the Initiative for MPTs (IMPT), a global learning network dedicated to advancing multipurpose prevention technologies (MPTs). Bethany served as a Peace Corps Volunteer in Mauritania, worked as an emergency refugee coordinator for UNHCR (Senegal), and had traineeships with the CDC (Ethiopia), the Institute Pasteur (Senegal), and the National Cancer Institute (Bethesda, MD). Bethany obtained her PhD in Epidemiology and MPH in Maternal and Child Health from the University of California Berkeley.

Pholo Maenetje

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Pholo Maenetje holds a PhD in immunology and is currently employed as a Senior Scientist at the Aurum Institute Clinical Research Division in Rustenburg, South Africa. Maenetje is a Principal Investigator of a Strategic Health Innovation Partnerships (SHIP) unit of the South African Medical Research Council (MRC)-funded grant that aims to understand the role of CD4 and CD8 αβ T cells and γ9δ2 T cells in protective TB immunity in the context of household contacts that remain persistently uninfected with TB despite repeated exposure to TB. The rationale is that identifying immune mechanisms that prevent or control and eliminate transient infection with Mycobacterium tuberculosis in individuals that remain persistently TB uninfected will provide insights on the mechanisms of protection conferred by adaptive immune responses and to use this information to develop effective TB vaccines and therapeutic strategies to prevent TB infection. Maenetje is also overseeing two observational studies funded by the International AIDS Vaccine Initiative (IAVI); one evaluating the feasibility of enrolling adolescents and assessing the uptake of essential health services within an adolescent friendly clinical trial setting, the other study that aims to evaluate the clinical, laboratory, immunologic and viral markers of disease progression in volunteers with recent HIV infection. He is also overseeing an NIH-R01 funded observational study that aims to explore the relationship between ART initiation and changes in lung structure and function. Pholo co-leads MATRIX's Capacity Strengthening, Engagement and Mentorship (CaSE) activity hub.

Wanzirai Makoni

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Wanzirai Makoni is Data Manager for MATRIX at Pangaea Zimbabwe AIDS Trust (PZAT) and a MATRIX Design2Delivery Hub Scholar for social and behavioural research. Her learning goal is to build expertise in social behavioral research on acceptability of and preferences for biomedical HIV prevention and to develop the skills to critically review this literature. She holds a Master of Public Health degree. In her career in research, she has coordinated studies ensuring ethics and regulatory compliance, conducting qualitative data collection and analysis, dissemination of results and study close-out. She has a keen interest in research and development of new HIV prevention delivery technologies including multi-purpose. Additionally, she has experience coordinating studies investigating product acceptability and adherence among women and health care providers.

Mutsumi Metzler

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Mutsumi Metzler, MBA, is Director, Commercialization in Medical Device and Health Technology Program at PATH based in Seattle, Washington. Ms. Metzler directs and manages the commercialization, market shaping, and introduction of medical, pharmaceutical, and diagnostic products and technologies. Her responsibilities include identifying and managing relationships with commercialization partners and public- and private-sector collaborators; negotiating agreements to develop, assess, and/or transfer technologies; conducting market research to ascertain market/stakeholder dynamics and estimate demand; and developing product commercialization and introduction strategies based on research results. She serves as a Co-Lead of MATRIX's Business, Market Dynamics and Commercialization Hub (BACH).

Alexandra Minnis

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Alexandra Minnis, PhD**,** is an epidemiologist and director of the Women's Global Health Imperative research program at RTI International. Her research addresses the prevention of HIV, STIs and unintended pregnancy, with a focus on social and structural influences on reproductive health in women and adolescents. Dr. Minnis has expertise in end-user research on biomedical HIV prevention and multipurpose prevention technologies, epidemiologic research methods applied to HIV prevention clinical trials, and research to elucidate and intervene on multi-level factors that contribute to reproductive health disparities. Her research approach integrates quantitative and qualitative methods and uses community-engaged participatory principles in design and implementation. Within MATRIX, she is Co-Lead of Social Behavioral Research in Clinical Trials, a Pillar within the Design to Delivery Hub, and protocol co-chair.of the MATRIX-002 study assessing the acceptability and safety of two placebo prototype monthly vaginal films.

Definate Nhamo

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Definate Nhamo is Senior Programs Manager, Pangaea Zimbabwe AIDS Trust (PZAT) and has been MATRIX's Design to Delivery Stakeholder Engagement and end-user research Country Co-Lead (Zimbabwe). She holds an MSc in Strategic Management and a BA hons in Sociology, and is currently completing her PhD. She has spent over two decades working on increasing access to Sexual Reproductive Health services (SRH) including HIV prevention options in research, implementation science and program delivery settings. She was the 2014 AVAC fellow for Zimbabwe and her work continues to focus on improving SRH to young women including HIV prevention technologies. She is very passionate about improving SRH access as well as expanding access of new HIV prevention technologies (oral PrEP and vaginal rings and injectables) to young women. She is involved in the Global Fund and PEPFAR processes in Zimbabwe. She is a member of the HPTN scientific committee and is passionate about scaling up proven interventions from research to roll out. She is currently the Zimbabwe deputy lead for another USAID-funded project – MOSAIC/CATALYST implementation science study.

Daisy Ouya

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Daisy Ouya joined AVAC in 2017 where she is currently Communications Manager: Research Engagement. As part of the USAID-funded CASPR project, Daisy's focus is research translation, stakeholder engagement, and communications in support of HIV prevention throughout the research to rollout continuum. Her 15-years-plus experience in science communications comes from working with international R&D non- profits as science editor, science writer, and communications specialist in diverse disciplines. Daisy has an MS in chemistry from the University of Connecticut, USA and a BSc in chemistry from the University of Nairobi in her native country, Kenya. She is also a board-certified Editor in the Life Sciences (ELS, USA).

Sravan Kumar Patel

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Sravan Patel, MS, PhD, is Assistant Professor of Pharmaceutical Sciences at the University of Pittsburgh School of Pharmacy and an investigator at Magee-Womens Research Institute. Dr. Patel is co-investigator in Lisa Rohan's lab and involved with development of novel drug products against HIV, herpes, and unintended pregnancy, as well as developing in vitro tools and models to assess product quality. Dr. Patel's goal is to address a variety of women health needs using innovative drug delivery and diagnostic solutions that are translatable, affordable and easy to use.

Sinazo Pato

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Sinazo Pato is Advocacy and Partnerships Manager for the International Partnership for Microbicides (IPM) South Africa NPC, an affiliate of the Population Council, where she oversees implementation of a program designed for the monthly Dapivirine ring outreach, education, and advocacy purposes in eastern and southern Africa. She has in-depth technical knowledge of HIV prevention tools from development to implementation such as PrEP, vaccines, microbicides, TaSP, and behavioral change interventions where she led community engagement function. Prior to joining clinical trials, Pato was a passionate activist advocating for access to affordable HIV treatment for all in South Africa. Pato participates in the regional leaderships roles aimed at strengthening inclusion of community voices in the development of HIV/AIDS policies. She is the chairperson of the Biomedical HIV Prevention Forum (BHPF) and member of the South African National AIDS Council Women Sector Leadership. Pato hold a Bachelors of Technology in Business Administration from the University of Johannesburg.

Krishnaveni (Surina) Reddy

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Surina Reddy is a Technical Head at the Wits Reproductive Health and HIV Institute (Wits RHI) Research Centre Clinical Research Site in Johannesburg, South Africa. She has a Masters degree in Medical Science and is currently pursuing her PhD. In her tenure as a research scientist (since 2005), her positions have included laboratory coordinator, regulatory compliance officer, study coordinator and programme manager for a number of clinical trials/studies pertaining to the evaluation of novel biomedical agents for HIV prevention (gels, oral pills and vaginal rings) as well as STIs and contraceptives among adult women, adolescent girls, young women and adult men (cisgender and transgender). Additional roles have included principal investigator (PI), Co-PI and Sub-investigator. During this time, she has gained significant experience with laboratory coordination, ethics and regulatory submissions and activation, implementation and close-out of National Institutes of Health-funded clinical trials network studies, particularly studies conducted by the Microbicide Trials Network (MTN). For MATRIX, Surina is protocol co-chair of the MATRIX-003 study evaluating two placebo prototype vaginal rings.

Lisa Rossi

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Lisa Rossi is director of communications for MATRIX and based at Magee-Womens Research Institute (MWRI) in Pittsburgh, Pennsylvania, USA, and for one year, also served as co-lead (Prime) for Stakeholder Engagement within the Design to Delivery activity hub. Lisa joined MATRIX after serving 15 years as director of communications and external relations for the Microbicide Trials Network (MTN), a National Institutes of Health-funded HIV/AIDS clinical trials network. Prior to working in HIV prevention, she managed media relations for the University of Pittsburgh Medical Center and University of Pittsburgh's six Schools of the Health Sciences, responsible for some of the university's most visible program areas, including 15 years leading media relations for its internationally renowned organ transplantation program during an era of medical firsts.

Francis Matthew Simmonds

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Francis Simmonds is a public health professional with experience in HIV prevention programming, particularly focusing on research, monitoring, evaluation, capacity strengthening, stakeholder engagement and costing. He is currently a Project Coordinator with the Pangaea Zimbabwe AIDS Trust (PZAT), supporting MATRIX's stakeholder and end-user engagements. Francis has a passion for data utilization for program improvement and to influence policy. He holds a Masters in Public Health, an MSc in Health Economics and a BSc (Hons) in Operations Research and Statistics.

Leonard Solai

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As Vice President, Global Product Access & External Affairs for the Population Council (Cape Town, South Africa), Leonard Solai leads the global product access program to ensure that the first long-acting, woman controlled, HIV prevention product, the dapivirine vaginal ring, is available and accessible to women where it's urgently needed. Solai has more than 25 years of experience working in the public health sector across multiple African countries. He has cultivated longstanding relationships with a variety of stakeholders working in HIV/AIDS and sexual and reproductive health and rights, including advocates, civil society, media, governments, and donors in the southern and eastern African countries most affected by HIV/AIDS. During his 15-year tenure at the International Partnership for Microbicides, an affiliate of the Population Council, he has leveraged these relationships to build a conducive environment for microbicide research and currently, for product introduction and access. Prior to joining IPM, he led large scale knowledge, attitudes, perceptions, and behavioural studies in response to the MDR / XDR TB outbreaks in southern Africa and then worked with public health organizations to design regional interventions. Solai has also led product introduction programs for antimalarial drugs in central and western Africa. Solai holds a Bachelor of Science in Medicine (Honours) degree, and a Master of Business Administration degree from the University of Cape Town, South Africa and Erasmus University, Netherlands.

Chelsea Solmo

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Chelsea Solmo is a Health Science Specialist at the United States Agency for International Development and Alternate Agreement Officer Representative for MATRIX. Before joining USAID, Chelsea was an Epidemiologist in the Office of the US Global AIDS Coordinator (S/GAC), working as the PEPFAR Program Manager for Ethiopia. Prior to S/GAC, Chelsea worked as a researcher for Columbia University's ICAP where she was the survey coordinator for the Population-Based HIV Impact Assessment (PHIA) in Eswatini, Malawi, Namibia, Ethiopia, and Uganda. She has also worked for the International Rescue Committee, the Clinton Health Access Initiative and for the United Nations Foundation. Chelsea has spent time overseas living and working in both Uganda and Bangladesh and spending significant time in India, Tanzania and in Eswatini where she helped lead the ECHO trial. She has an MPH from Johns Hopkins University in Global Epidemiology and a B.A. from the University of Florida in Biology. Outside of work, Chelsea enjoys reading, playing with her two cats and exploring her city and other countries one restaurant at a time.

Ariane van der Straten

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Ariane van der Straten holds a PhD in Molecular Biology, and an MPH in International Health. She currently is an Adjunct Professor at the University of California San Francisco (UCSF) School of Medicine, and an independent consultant through ASTRA consulting. Since 1993, she has conducted research on women's sexual and reproductive health globally, focusing on developing new products to prevent HIV. Her expertise spans preclinical (from in vitro to macaque studies), clinical (phase I-III trials) and socio-behavioral (end-user-centric qualitative and quantitative) research to evaluate short and long-acting HIV prevention strategies (topical, oral, injectable, or implantable), and multi-purpose prevention technologies (MPTs). Ariane is a consultant to MATRIX Prime and she supports the management of the early product research and development portfolio for MATRIIX.

Betsy Tolley

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Betsy Tolley, PhD, is a Senior Scientist and Director of a behavioral and social science research group at FHI 360, in Durham, North Carolina, USA, and Co-Lead of End-User Product Preferences Research, a Pillar within MATRIX's Design to Delivery Hub. She employs a range of research methodologies (qualitative, quantitative, scale development and human-centered design approaches) to examine the acceptability of and adherence to contraceptive, HIV prevention and multipurpose prevention technologies. Betsy has a PhD in Health Behavior from the University of North Carolina-Chapel Hill and a MA in International Development from the Nitze School of International Studies, The Johns Hopkins. Betsy speaks fluent French, has a working knowledge of Hindi/Urdu and Arabic and over 30 years' experience living and working internationally.

Lynn Wang

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Lin Wang, a Research Manager in the Rohan Pharmaceutics Lab, obtained her B.S. and M.S. in Pharmaceutical Sciences from Shenyang Pharmaceutical University in China. With over a decade of experience in new drug product development, she is specialized in preformulation, formulation research and development for variable dosage forms including tablets, capsules, gels, emulsions, liposomes, films, suppositories, analytical quality control and assessment. She has worked on numerous projects involving vaginal/rectal microbicide product developments for a wide range of microbicide candidates, including hydrophobic, hydrophilic, and small molecules and proteins. Her expertise has contributed to bring new drug products from the bench to the clinic

Junmei Zhang

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Junmei Zhang is a Research Assistant Professor in the Department of Obstetrics, Gynecology & Reproductive Sciences at the University of Pittsburgh School of Medicine. She is also the project manager in Dr. Lisa Rohan's laboratory. Within MATRIX, she has been working with her team members since December 2021 on the development of two 30-day vaginal films for the prevention of HIV, and HIV and unintended pregnancy, respectively. Dr. Zhang received her PhD in analytical chemistry from the University of Texas at Austin, and her master's degree in pharmaceutical chemistry from Peking Medical University. She has expertise in bioanalytical chemistry, proteomics research, and pharmaceutical product development. She is also experienced in project management, scientific writing, regulatory compliance, and mentoring students/junior staff.

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

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