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MATRIX

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

About MATRIX

- MATRIX is a five-year program funded by the U.S. Agency for International Development (USAID) in 2021 that aims to expedite the research and development of HIV prevention products for women – including products 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 activities are primarily 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 aims also to strengthen the research and development capacity of African investigators to facilitate full and sustainable ownership of this work.

- MATRIX is being implemented by Magee-Womens Research Institute (MWRI) in collaboration with partner organizations based in Kenya, South Africa, the United States and Zimbabwe. Leading the project is Sharon Hillier, Ph.D., of MWRI and the University of Pittsburgh, USA, with Thesla Palanee-Phillips, Ph.D., from Wits RHI and University of Witwatersrand, South Africa, serving as deputy director. Collectively, MATRIX partners 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.

How is MATRIX unique?

- The research and development of new products begins with rigorous testing in the laboratory and then studies in animals seeking to demonstrate their potential safety and efficacy. These studies must be conducted, and other regulatory requirements met, before a product can proceed to human clinical trials. The products being developed under MATRIX must also meet a second set of standards that considers what women want and are likely to use and whether the product will provide added value and be practical and feasible to introduce in countries most affected by HIV. Indeed, a key feature of MATRIX is its focus on being responsive to end-user and stakeholder feedback during the earliest stages of product development to inform decisions about product design and MATRIX's overall research agenda.

- While early-phase clinical trials of new HIV prevention products have predominately been conducted in the United States or Europe, MATRIX is conducting these kinds of studies in sub-Saharan Africa (in parallel with the United States) in order to gain important insight into the safety and acceptability of new products in the populations that are most important.

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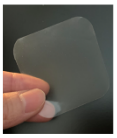
The MATRIX Product Pipeline and Clinical Studies

- MATRIX's primary focus is on the early development of HIV prevention products for women, including dual-purpose products that would also protect against unplanned pregnancy. MATRIX seeks diversity in the products it supports, whether it be short-acting vaginal products to be used at the time of sex, products to be used for a month at a time or systemic products that could potentially provide protection for up to a year. Products may be new formulations of existing antiretroviral (ARV)-based methods, while others contain novel antiviral agents.

- Early research and development is an unpredictable process – a product that initially appears promising can face insurmountable challenges at any point along the way. MATRIX takes an approach that prioritizes those products that have the greatest chance for success and to add value by setting clear milestones and benchmarks and being responsive to technical hurdles and/or developments within the broader field. As such, the MATRIX pipeline of products is dynamic. In 2022, MATRIX was supporting six products, then the product pipeline expanded to nine products in 2023. The current portfolio (*see table below*) includes four products, and this, too, could change should new products be added and/or further prioritization be necessary.

Product		Developer	Product Type	Active Ingredient(s)	How used	Protection Goal	Unique Features/ Additional Information	Development Status
	**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**	TAF has also shown activity against HSV, which could be added benefit.. Outside of MATRIX, CONRAD is also evaluating use of the insert rectally.	**MATRIX-001** is evaluating safety and acceptability of insert at sites in Kenya, South Africa & US –the first Phase 1 study in African women..
	**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 dual-purpose product*	**MATRIX-002** is evaluating acceptability and usability of 2 placebo films at sites in Kenya, South Africa, Zimbabwe & US. Will determine film to be used in first-in-human trial of monthly dapivirine film.
	**Dapivirine & levonorgestrel dual-purpose vaginal film**	**Univ of Pittsburgh** (USA)	**Vaginal film (dual purpose)**	**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**
	**Non-ARV/ nonhormonal contraceptive dual-purpose vaginal ring**	**Oak Crest Inst of Science** (USA)	**Vaginal ring (dual purpose)**	**Antiviral peptide** *(protein fragment –non-ARV)* **soluble Adenylyl Cyclase (sAC) inhibitor** *(non-hormonal contraceptive)*	**Women insert themselves**	**1 month**	The antiviral also shows activity against HSV and HPV, which could be an added benefit. The sAC inhibitor affects sperm's ability to move, fertilize eggs	**MATRIX-003** is evaluating acceptability of 2 placebo rings at sites in South Africa, Zimbabwe & US. Will determine product design to be evaluated in clinical trials with active drug.

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- MATRIX currently has three ongoing studies: MATRIX-001, a Phase 1 trial of the TAF/EVG fast-dissolving insert in women at sites in the U.S., Kenya and South Africa – the first study of the insert in African women; MATRIX-002, which is evaluating the acceptability and usability of two prototype films (with no active drug) designed to dissolve over the course of a month among women at sites in the U.S., Kenya, South Africa and Zimbabwe – the first study of a 30-day vaginal film; and, MATRIX-003, a similar study that's evaluating two prototype vaginal rings that women would use for a month at a time, with sites in the U.S., South Africa and Zimbabwe. Both the MATRIX-002 and MATRIX-003 studies will help inform the final design of the active products to be evaluated in first-in-human trials – a monthly vaginal film containing the ARV dapivirine and a dual-purpose monthly vaginal ring containing a non-ARV and a nonhormonal contraceptive, respectively.

- Among its planned studies is MATRIX-007, or CARE-PrEP (Cabotegravir, Oral PrEP and Ring Evaluation in Pregnancy), which intends to collect high quality safety data among participants in the CATALYST study who become pregnant while using an ARV-based prevention product – cabotegravir long-acting injection (CAB-LA), monthly dapivirine vaginal ring or daily oral pre-exposure prophylaxis (PrEP) – and elect to continue its use during pregnancy. MATRIX-007 will be conducted in collaboration with Maximizing Options to Advance Informed Choice for HIV Prevention (MOSAIC), a five-year program funded by the U.S. President's Fund for AIDS Relief through USAID.

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