

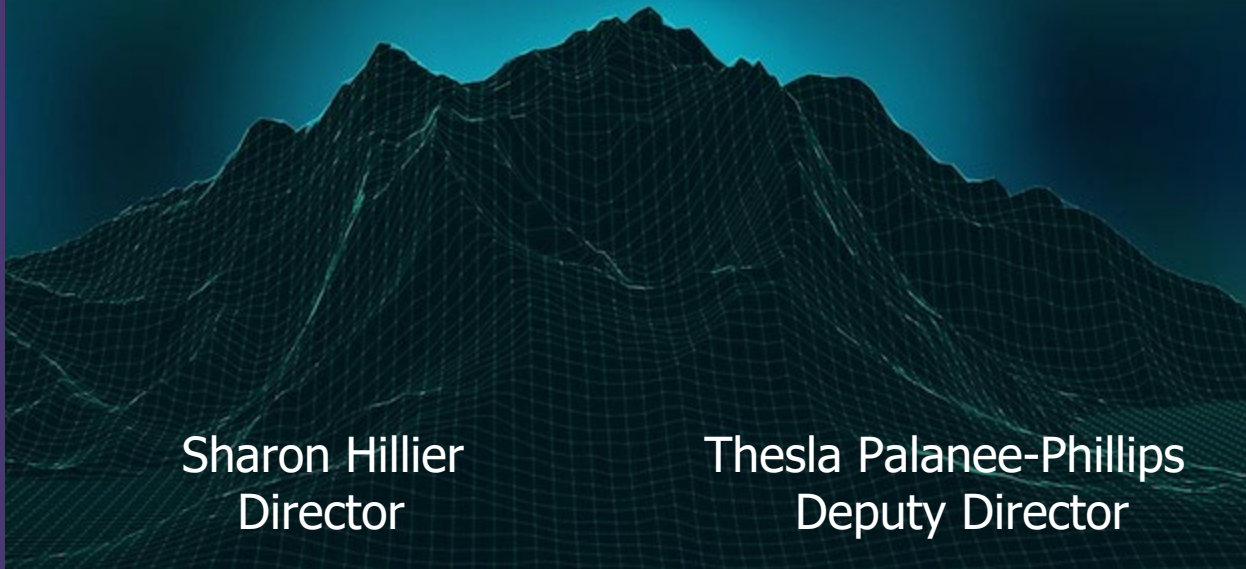
The red pill and blue pill represent a choice between *the willingness to learn a potentially unsettling or life-changing truth* by taking the *red pill* or *remaining in the contented experience of ordinary reality* with the *blue pill*.

The terms originate from the 1999 film The Matrix.



MATRIX

The Mountain we are climbing



Sharon Hillier
Director

Thesla Palanee-Phillips
Deputy Director



*the willingness to learn a potentially unsettling or life-changing truth by taking the **red pill***



Reflections on the past 1.5 years

- MATRIX submission ~24 months ago (September 15, 2021)
- MATRIX funded by USAID on December 1, 2021
- We had a plan...and we were adaptable – Co-creation!
 - What have we accomplished?
 - What has worked?
 - What has been complicated?
 - What is our plan for the rest of this year and year 3?



Project Overview

Five year, \$125 million Cooperative Agreement

- Funded by the U.S. Agency for International Development (USAID)
- Implemented by Magee-Womens Research Institute and Foundation (MWRIF) with 17 implementing partners in South Africa, Kenya, Zimbabwe and the US

Project Goal: Develop a range of HIV prevention products which are **acceptable, affordable, scalable, and deliverable** and **meet the unmet needs** of women at risk of HIV infection through **equitable North-South partnerships** and rigorous evaluation of project research and development (R&D) activities



The MATRIX mantra

Develop a *range of HIV prevention products* that are:

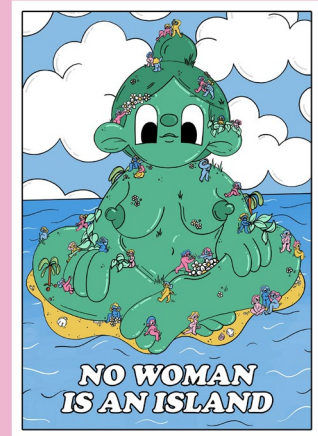
- **Acceptable:** integration of **end-users and stakeholders'** feedback from the earliest stages of product development and the deliberate intention to conduct early-stage clinical trials in Sub Saharan Africa to gain early insights on the acceptability of HIV prevention products.
- **Affordable** : Making products more **affordable** by **extending efficacy windows**, reducing costs from clinic visits, employing non-ARV based options to **reduce costs/burden** of HIV testing and leveraging scalable low-cost technologies.
- **Scalable** : Products prioritized which can be scaled up locally for **manufacturing** and issues such as **product stability and cold chain requirements** have been considered.
- **Deliverable:** MATRIX proposes an integrated program to gain input from Ministries of Health and SSA governmental bodies early **in product development** to meet needs of those in the Global South

Putting Women at the Center of HIV Prevention Research—and Beyond



No woman is an island : Lived realities

- Women exist in a continent, in a country, society, in a family and in a home
- Influencers, barriers and facilitators for every decision – reverse *ripple* effect
- **Regional** – what are regional norms
- **Country** – infrastructure, affordability, availability, policies, complications
- **Societal** – how do key influencers impact providers buy in, provider burden and fatigue, support is crucial
- **Individual** – priorities, values, preferences, choice, duties, responsibilities, ebbs and flow of life expectations

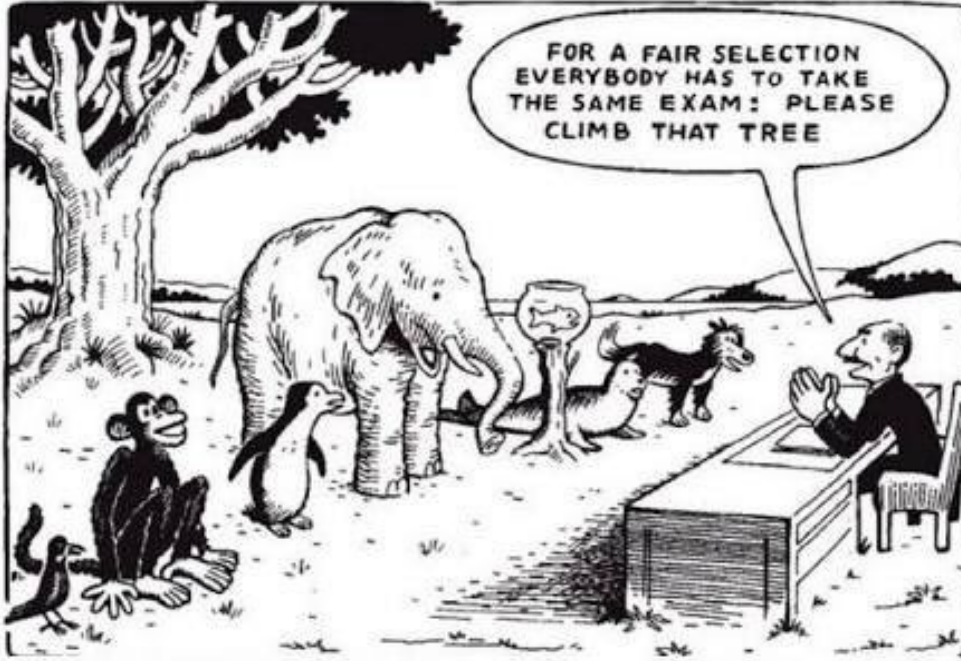


Challenges and barriers for women at Risk of HIV/STIs

- **Biological susceptibility** : physiological
- **Behavioural issues** : Age-disparate sex, multiple partnerships, transactional sex, early sexual debut, gaps in knowledge and **limited personalized risk perception**.
- **Structural** : Harmful social and gender norms, gender inequality and power dynamics, barriers to accessing SRH and HIV services, Gender based violence



Each woman has her own set of barriers and facilitators that impact her **willingness and ability** to use HIV prevention options



CONTEXT
MATTERS

**A one size fits all
approach does not work**

acceptable, affordable, scalable, and deliverable

MATRIX

Our beautiful MATRIX countries



**Johannesburg,
Durban, South Africa**



**Nairobi, Kenya
Harare, Zimbabwe**



Our beautiful MATRIX cities



Kenya



Our beautiful MATRIX cities



Zimbabwe, Chitungwiza



Our beautiful MATRIX cities



South Africa:
Durban



Our beautiful MATRIX cities



South Africa: Vulindlela, Pietermaritzburg

Our beautiful MATRIX cities



South Africa: Johannesburg



SA public healthcare



Why MATRIX?

Choice is an illusion created
between those with power and
those without.

FLANEUR



acceptable, affordable, scalable, and deliverable

MATRIX

REMINDER : The MATRIX mantra

Develop a *range of HIV prevention products* that are:

- **Acceptable:** integration of **end-users and stakeholders'** feedback from the earliest stages of product development and the deliberate intention to conduct early-stage clinical trials in Sub Saharan Africa to gain early insights on the acceptability of HIV prevention products.
- **Affordable** : Making products more **affordable** by **extending efficacy windows**, reducing costs from clinic visits, employing non-ARV based options to **reduce costs/burden** of HIV testing and leveraging scalable low-cost technologies.
- **Scalable** : Products prioritized which can be scaled up locally for **manufacturing** and issues such as **product stability and cold chain requirements** have been considered.
- **Deliverable:** MATRIX proposes an integrated program to gain input from Ministries of Health and SSA governmental bodies early **in product development** to meet needs of those in the Global South

What is Happening with the PDs?

How these new products game-changers?






- You will be hearing from each product developer today and tomorrow: what they are developing, why they are developing it and the gap it will fill in the prevention landscape



MATRIX Product Pipeline Overview

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)	FDI	TAF/EVG <i>tenofovir alafenamide & emtricitabine</i> <i>NRTI & integrase inhibitor (ARVs)</i>	On-demand <i>(women insert themselves at or around time of sex)</i>	Up to 3 days	TAF has also shown activity against HSV, which could be added benefit. CONRAD also evaluating the insert's rectal use.	MATRIX-001 to evaluate the safety and acceptability of insert at sites in Kenya, South Africa & US – the first Phase 1 study in African women. Expected start 2023.
2		Griffithsin Fast-dissolving vaginal insert	Population Council (USA)	FDI	Griffithsin antiviral protein (non-ARV) <i>Viral entry inhibitor</i>	On-demand <i>(women insert themselves at time of sex)</i>	4-8 hours	Animal and laboratory studies indicate Griffithsin also has activity against HPV and HSV, which could be added benefit.	Pre-clinical
3		Dapivirine vaginal film	Univ of Pittsburgh (USA)	Vaginal film	Dapivirine <i>NNRTI (ARV)</i>	Women insert themselves	1 month	Film would slowly release drug until it completely dissolves. <i>Also being developed as dual-purpose product</i>	MATRIX-002 to evaluate acceptability and usability of 2 placebo films at sites in Kenya, South Africa, Zimbabwe & US. Expected start 2023; will determine film to be used in first-in-human trial of monthly dapivirine film.
4		Cabotegravir hydrogel injectable	CONRAD (USA)	Inj depot	Cabotegravir <i>Integrase strand inhibitor (ARV)</i>	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, removable in first month) <i>Also being developed as dual-purpose product</i>	Pre-clinical
5		Cabotegravir dissolvable pellets	CONRAD (USA)	Pellet implant	Cabotegravir <i>Integrase strand inhibitor (ARV)</i>	Inserted under skin	Up to 1 year	8-9 pellets would be inserted in a row that slowly release drug as they dissolve in course of a year. (If needed, removable in first 1-2 mos) <i>Also being developed as dual-purpose product</i>	Pre-clinical

MATRIX Product Pipeline Overview

Product	Developer	Product Type	Active Ingredient(s)	How used	Protection Goal	Unique Features/ Additional Information	Development Status
---------	-----------	--------------	----------------------	----------	-----------------	---	--------------------

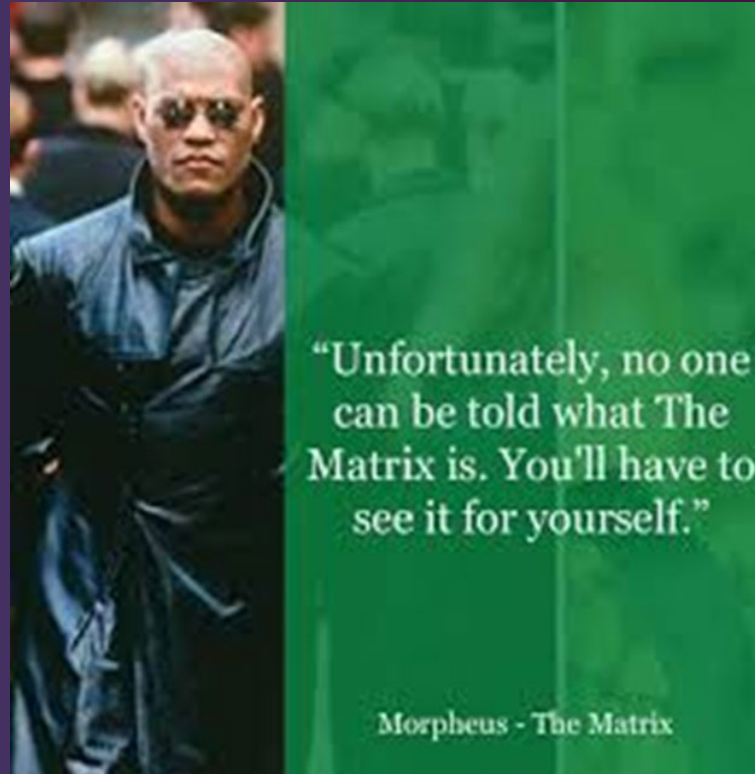
Products for Prevention of HIV and Pregnancy (Dual Purpose)

1		Non-ARV/ nonhormonal dual-purpose vaginal ring	Oak Crest Inst of Science (USA)	Vaginal ring	Antiviral peptide (non-ARV) (protein fragment) Non-hormonal contraceptive <i>A soluble Adenylate Cyclase (sAC) inhibitor; affects sperm's ability to move, fertilize eggs</i>	Women self insert	1-3 months	The antiviral also shows activity against HSV and HPV, which could be an added benefit.	MATRIX-003 to evaluate acceptability of 2 placebo rings at sites in South Africa, Zimbabwe & US. Expected start 2024. Will determine ring to be evaluated in first-in-human trial of active ring.
2		Dapivirine and levonorgestrel vaginal film	Univ of Pittsburg h (USA)	Vaginal film	Dapivirine <i>NNRTI (ARV)</i> Levonorgestrel (LNG) <i>hormonal contraceptive</i>	Women self insert	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 <i>Integrase strand inhibitor (ARV)</i> Levonorgestrel (LNG) <i>hormonal contraceptive</i>	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)	Pre-clinical
4		Cabotegravir/ levonorgestrel dissolvable pellets	CONRAD (USA)	Pellet implant	Cabotegravir <i>Integrase strand inhibitor (ARV)</i> Levonorgestrel (LNG) <i>hormonal contraceptive</i>	Inserted under skin	Up to 1 year	8-9 pellets would be inserted in a row that slowly release drug as they dissolve in course of a year. (If needed, could be removed in first 1-2 mos)	Pre-clinical

We use a lot of terms
in MATRIX!

One of the goals for
today is to help you
learn what some of
those terms mean.

And there will be
quizzes along the way...



A reminder of how MATRIX is structured: 5 Activity Hubs to Support the PDs

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
- Designs and implements behavioral studies & socio-behavioral research within trials
- Seeks stakeholder feedback on products, proposed studies and regulatory process.

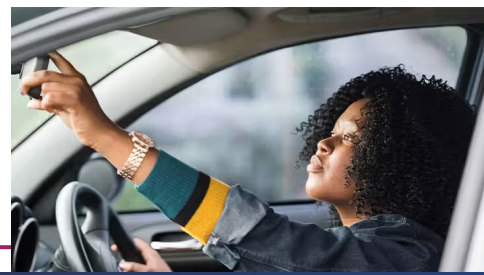
Business, Market Dynamics and Commercialization (BACH)

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

Capacity Strengthening, Engagement and Mentorship (CaSE)

- Matches African investigators with early R&D mentorship and fellowship opportunities

What is D2D?



- **Deciding 2 Drive**
- **Determined 2 create Demand**
- **Design to Delivery Hub:** a pathway for early input into product design from a broad range of potential end-users stakeholders through to PDs via an iterative **Research Feedback Loop**

Demand Creation:
The Key to a New Product's
Commercial Success

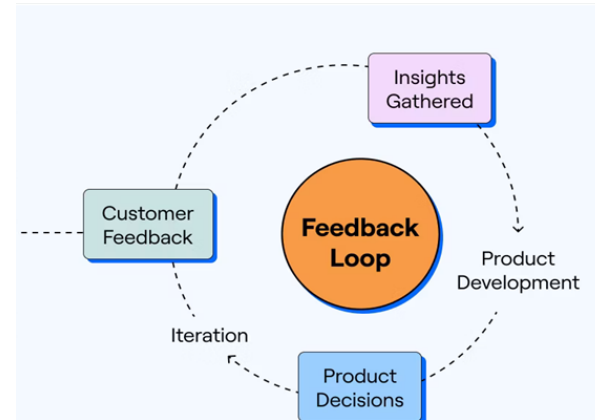


D2D Pillar 1 conducts social behavioral research outside of clinical trials
D2D 2 conducts social behavioral research within MATRIX clinical trials
You will hear about this work on Wednesday

MATRIX Research Feedback loop

Why is it so important ?

Active listening, hearing and supported synthesis of findings and informed incorporation is crucial to our PDs and Critical path products success!



Goal : Inform development of products that are acceptable, affordable, scalable and deliverable !

What is CaSE?

- **C**ats and their **S**urprising **E**scapades
- **C**ars: **S**edans and **E** Class Mercedes Benz
- **C**apacity **S**trengthening and **E**ngagement
- CaSE matches African investigators with mentorship and fellowship opportunities, with an emphasis on early R&D
- You will hear more about this tomorrow



What is BACH?



- A famous composer
- **B**eautiful **A**ctresses **C**alling to be **H**ired
- **B**usiness, **M**arket Dynamics, and **C**ommercialization **H**ub
- BACH's goal is to support MATRIX product developers in identifying and fostering collaboration with potential public- and private-sector resources and generating evidence to ensure sustainability and long-term impact
- BACH is co-led by PATH, Aurum Institute and IAVI, in partnership with PHI.



So how does it all fit together?

- **Product developers** work independently on getting their products to the point that they can be tested in **clinical trials**.
- **Hubs** support the **product developers** through provision of expertise (**Tech Accelerator** or **Clinical Trials Hub**, providing social behavioral feedback at early stages of development (**D2D**), help make a business case (**BACH**) and ensure that we are supporting growth of research capacity in Africa (**CaSE**)



Decide on a Restaurant Idea:

- ✓ Secure a business location
- ✓ Apply for Licenses and Permits
- ✓ Buy Equipment
- ✓ Develop Menu ideas
- ✓ Sit down or fast food?
- ✓ Develop a business plan

Product Developers



Purchase Ingredients:

- Chicken Breast
- Spices for the sauce
- Chips or no chips?
- Flour
- Buns
- Pickles
- Lettuce
- Tomatoes
- Condiments



Test Kitchen:

- Taste different prototypes
- Adjust ingredients, techniques, and cooking times
- Does the process work well?

Clinical Trials



Advice from potential restaurant visitors:

- What are they looking for?
- What kinds of things do they like or not like about spicy food like sandwiches?
- Would they go to this restaurant?

D2D Pillar 1



Work with Consumers who ate the sandwich in the test kitchen:

- How do they feel after eating the spicy chicken sandwich?
- Bad breath?
- Indigestion?

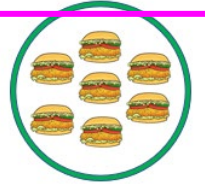
D2D Pillar 2



Work with Communities and Stakeholders:

- How do they feel about having more spicy chicken sandwich shops in the vicinity?

D2D Pillar 3 and Prime



How can we ensure that there are people available to manage the restaurants and solve problems which will arise in different settings?



Is there a business case to create a chain of restaurants for Africa? Who can invest in this? What will the costs be? Will the new restaurants be competitive?



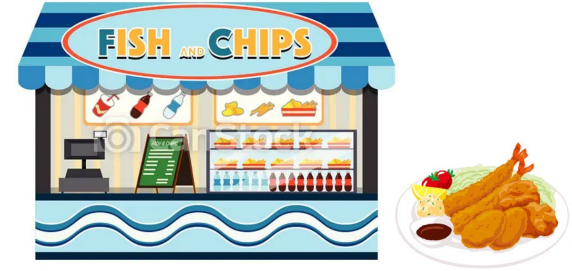
TAF/EVG Inserts



Non hormonal/non-ARV ring



CAB insert and implantable pellets



Monthly film



GRFT FDI



It is Complicated But It Can Make Sense



What? Complicated?

- Four different Product Developers
- Nine different products
- Scientific Advisory Group for monitoring PD progress
- Portfolio assessment review tool

- Five activity hubs, each doing very different things but trying to understand *what everyone else* is doing

- Aggressive timelines with frequent reporting
- Being quick and adaptable also means that we are refining and changing our approaches constantly



What Has Worked in MATRIX?



THE MATRIX 4

WHAT WE KNOW
SO FAR

- **We have!**
- As a group we have worked tirelessly to figure out:
- **Who** everyone is (via Zoom and MS teams)
- **What** the expectations are
- **How** to work together
- **When** are we expected to get it done
- **Why** we are doing it

We have accomplished a lot in our first 18 months!

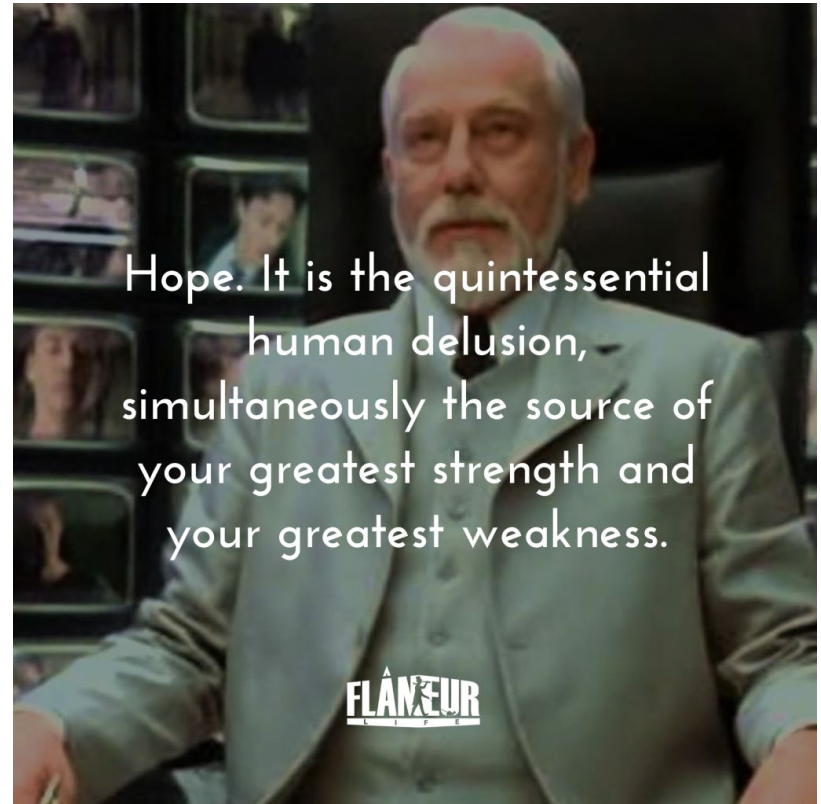
What Has Been Challenging?

- Multiple partners in multiple countries and multiple time zones, all with their own contexts, challenges, internal processes (sheer complexity of logistics for collaborative work and calls)



A reflection on MATRIX.....

- Lots of pain, many gains!
- We are privileged to conduct this work to expand the portfolio of new prevention products
- The teams are still building and getting to know each other. It takes time to build integrated and highly functioning teams
- Thanks to everyone for the blood, sweat and tears so far
- YOU are the “secret sauce” which will make MATRIX a success



A close-up shot of Morpheus from the movie 'The Matrix'. He is bald, wearing dark sunglasses and a green leather jacket. He is sitting in a red leather chair. The background is dark and out of focus.

“THERE'S A DIFFERENCE
BETWEEN KNOWING THE PATH
AND **WALKING** THE PATH.”

— *Morpheus, "The Matrix"*

Thank you for each walking this path

MATRIX

Acknowledgements

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

The contents in this presentation are those of the presenter and do not necessarily reflect the view of the U.S. President's Emergency Plan for AIDS Relief, the U.S. Agency for International Development or the U.S. Government.

