Stakeholder Feedback and Discussion
Critical Pathway Products:
Regulatory, Cost & Manufacturing Considerations

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30 August 2024 – Nairobi, Kenya

PEPFAR
U.S. President's Emergency Plan for AIDS Relief

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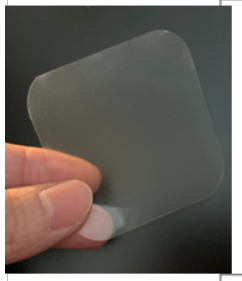
MATRIX
Advancing R&D of Innovative
HIV Prevention Products for Women

MATRIX current product pipeline

Product	Developer	Product Type	Active Ingredient(s)	How used	Protection Goal	Unique Features/ Additional Info	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 time of sex)*	**At least 1 day**	TAF shows activity against HSV- may be added benefit. . Outside of MATRIX, CONRAD evaluating as rectal insert.	**MATRIX-001** – safety and acceptability Phase 1 study (US & African sites)..
 **Dapivirine vaginal film**	**Univ of Pittsburgh** (USA)	**Vaginal film**	**Dapivirine** *NNRTI (ARV)*	**Women insert themselves**	**1 month**	Film would slowly release drug as it dissolves. *Also being developed as dual-purpose*	**MATRIX-002** – safety, acceptability & usability of 2 placebo films (US & African sites) –informing film design for first-in-human trial of active product.
 **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**	Film would slowly release dapivirine and LNG as it dissolves	**Pre-clinical**
 **Non-ARV/ nonhormonal contraceptive dual-purpose vaginal ring**	**Oak Crest Inst of Science** (USA)	**Vaginal ring** ***(dual purpose)***	**Antiviral peptide** *(protein fragmen -non-ARV)* **soluble Adenylyl Cyclase (sAC) inhibitor** (*non-hormonal contraceptive*)	**Women insert themselves**	**1 month**	Antiviral shows activity against HSV & HPV- may be added benefit. sAC inhibitor affects sperm's ability to swim	**MATRIX-003 –** acceptability of 2 placebo rings (US & African sites) – deciding ring for first-in-human study of active product.

Stakeholders attending our regional consultation last year recommended that our product developers seek pre-IND-like meetings with African regulators, and representatives from the regulatory authorities in Zimbabwe and South Africa indicated they had processes for doing so.

- What are the views of the Pharmacy and Poisons Board and others in this regard? Are you open to engagement now, i.e., early in the drug development process?
- Are processes in place for such engagement?

MATRIX product developers plan to follow a development pathway defined by the US FDA. This brought about much discussion at our last consultation – stakeholders felt that the FDA as a primary pathway is no longer considered acceptable or ideal.

What they said

"… 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.** … As much as we recognize the work done by FDA, **as we do reliance, we still need the full data**."

Mphako Ratlabyana
Manager, Pharmaceutical Evaluation and Management Pre-Registration Unit
SAHPRA (South Africa)

"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 if 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, KEMRI
Chair, Bioethics Society of Kenya

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What they said

"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

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It was strongly recommended that product developers should seek a regulatory pathway that includes the African Medicines Agency (AMA), either in parallel with the FDA or in some collaborative manner.

- Do you agree?
- How do you expect to interface with the AMA?

Some of our products are quite novel. Those incorporating new APIs and/or contraception may come as a challenge when it comes to ethics and regulatory reviews, especially as we embark on first-in-human studies.

- What are your views of AVAREF (African Vaccine Regulatory Forum) as a vehicle for joint review of protocols, which as a technical committee for the AMA, its mission is to strengthen ethics and regulatory capacity for clinical trials ensuring oversight of product development in African countries?
- Do you have experience with this process?

- What should product developers be thinking about and doing now – at this early stage – to address potential concerns about costs of goods and delivery?
- Are there considerations related to packaging or labeling?
- Is local manufacturing feasible, in your view?