MATRIX-002: A Study to Assess the Acceptability and Safety of Two Placebo Prototype Vaginal Films

Protocol co-chairs

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MATRIX-002: Background

- HIV acquisition among young women – especially in SSA - continues to be unacceptably high.
- HIV prevention OPTIONS are needed
    - Oral PrEP is the only biomedical prevention option (other than condoms) currently widely available; not everyone wants or is able to follow a daily regimen
    - A monthly vaginal ring (dapivirine ring) and an injection given every two months (CAB-LA) are not yet widely available
- With contraceptives, evidence indicates that with more options available use increases overall.

Vaginal films are being developed as a novel HIV prevention tool.

Product Developer: University of Pittsburgh/ Magee-Womens Research Institute and Foundation

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Why use placebo products in a clinical trial?

- Inform key design decisions before Phase I.
- Focus on product attributes of a drug delivery system, irrespective of the drug formulation.
- Evaluate insertion instructions and counseling to inform future materials for clinical trials and implementation.

Quatro study vaginal film input: Women, partners, and key informants

Positive attributes	Negative Attributes	Current MATRIX Study
Female initiated*** (W,MP,KI)	Difficult to insert** (W, MP, KI)	Insertion instructions updated
Tightened vagina & enhanced sexual pleasure*** (W,MP)	Takes long to dissolve/disrupts sex** (W,MP,KI)	New formulation will be evaluated for dissolution timing and impacts on sex
Small** (KI)	Plastic** (KI)	
Allows barrierless sex* (KI)	Short-term use** (W,MP,KI)	Duration extended to 1 month
Discreet* (KI)	Method of insertion unhygienic* (W,KI)	Insertion experience and acceptability will be examined (including desire for applicator)
Doesn't disturb sex* (W,MP)	Scratching corners during insertion* (W,KI)	Film with rounded corners will be evaluated
Easy/painless to insert** (W,KI)	Made vagina too wet* (W)	
Dissolves* (W,KI)		

Source: Musara P, et al. *AIDS Behav*, 2021.

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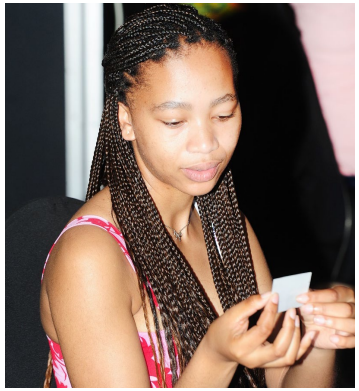
MATRIX-002: Input from stakeholders



- Placebo films were passed around at 2022 stakeholder consultations in South Africa, Zimbabwe and Kenya
- Across all three meetings, the film's size and shape generated the most comments – the **corners were seen as too sharp**
- Stakeholders in Zimbabwe seemed less taken aback – perhaps because a former QUATRO participant was able to dispel notions that it was difficult to insert, didn't remain in place or could be felt by partners

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MATRIX-002: Study overview

- A study that **will assess the acceptability and safety of two monthly placebo vaginal films** containing no active drug.
- The two films **differ in their shape** –rounded corners vs. straight corners.
- This is the **first study of a film designed to dissolve over a course of 1 month.**
- **Will determine the film design to be evaluated in a first-in-human study of a monthly film containing the ARV dapivirine.**
- Will also help to understand what support and counseling women need to use the film and how best to address questions and concerns that women and/or their partners may have about film use.

MATRIX-002: Study design

- Two-arm, randomized, multi-center trial - Women will be **randomly assigned** to use **one of the two placebo films.**
- Participants will use their assigned film twice – for 1-month each
  - During the **first month** of film use, women are to **refrain from sex and vaginal product use**
  - During the **second month** of film use, there are **NO restrictions**
  - Participants will **insert the films themselves** in the clinic each; Study staff will provide guidance and instructions
- Participants will undergo physical and pelvic exams and be asked questions about their experience and likes and dislikes with using the film
  - Up to 35 participants will also be asked to participate in an in-depth interview at the end of the study

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MATRIX-002: Study overview

Study Population - 100 participants and up to 30 sexual partners at **5 trial sites in 4 countries**

Kenya Kenya Medical Research Institute

South Africa
- Aurum Institute
- Wits RHI

Zimbabwe - Harare Health and Research Consortium

United States - University of Pittsburgh/Magee-Womens Research Institute

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MATRIX-002: Primary and secondary objectives

Primary Objective: Acceptability

- To assess the acceptability of two placebo film types (A and B) when administered vaginally once monthly for two months.

Secondary Objectives: Safety and usability

- To assess the safety of two placebo film types (A and B) when administered vaginally once monthly for two months.
- To assess participants' ability to properly insert the placebo vaginal film.

MATRIX-002: Exploratory objectives

Objectives will assess:

- Participant acceptability, attitudes and experiences (multiple dimensions)
- Sexual partner attitudes and experiences
- Vaginal microenvironment
- Social harms and social benefits

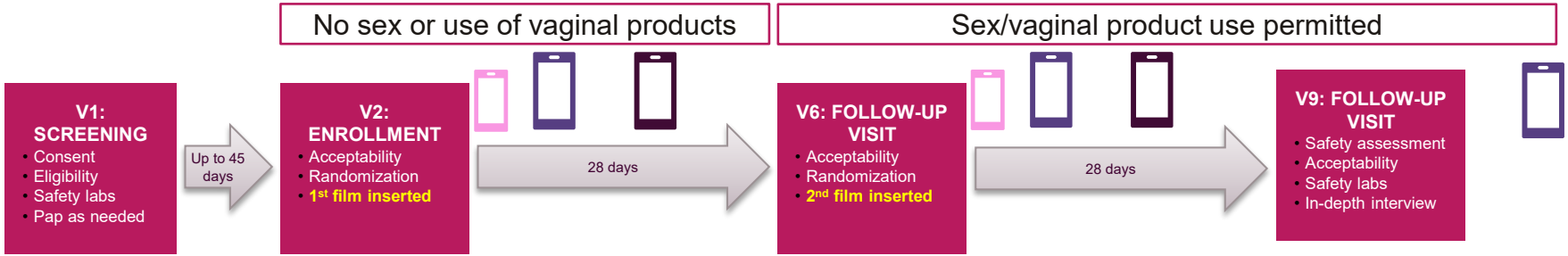
MATRIX-002: Study design

Pre- and post-insertion assessment at ENR and V6

Regular phone check-ins to have early and frequent touchpoints

SBR CRFs at each timepoint to systematically collect data on user experience throughout both months of product use

IDIs with participants and sexual partners to gain comprehensive understanding of product use experiences



= 24-72 hr phone check

= 1 week phone check

= 2 week phone check

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MATRIX-002: In-depth interviews (IDI)

- Up to 35 participants will complete an IDI
  - Involves a one-on-one interview with a trained researcher to gather more detailed information on the participant's use and thoughts about film use
  - IDIs will be audio recorded for transcription and analysis

MATRIX-002: IDIs with sex partners

- Participants will be asked if they would agree for their partner to be contacted to participate in an in-depth interview.
  - Participants sign a permission to contact the sexual partner
  - Up to **30 sexual partners** will be invited
  - Partner will sign an informed consent, if interested
  - In-depth interview conducted by socio-behavioral researcher (participant not present)

MATRIX-002: Illustrative questions

- **Acceptability**
  - Which film shape is more acceptable?
  - How do participants feel about using a monthly vaginal film?
  - Will sex or vaginal products/practice interfere with film use?
- **Safety**
  - What is the frequency of Grade 2+ product-related adverse events?
- **Usability**
  - Can women insert the vaginal films properly themselves?

MATRIX-002: Status update

- Study activation in progress
- Protocol training: 30 September, with SBR-specific training planned with site teams
- Regulatory approval applications at various stages at Univ of Pittsburgh, HHRC, KEMRI, and Wits RHI
- Study implementation materials under development
  - Activation checklists

MATRIX-002: Summary

- MATRIX-002 will provide **acceptability and safety data** on two different shapes of placebo monthly vaginal films
- MATRIX-002 will inform end-user and partner **education and counseling for future studies** with the vaginal film
- Findings will **inform the next version of the monthly vaginal film** which will include:
  a) an anti-HIV medication and
  b) a dual-purpose anti-HIV and a contraceptive (film)

Acknowledgements

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