30 Day Dapivirine Film

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

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Why film?

Ease of Use & Privacy:

Women control use and insertion of film

Can be used discreetly and inserted anytime in private

Not expected to impact sex

Unique & Convenient Platform:

Removal not required

Complete drug release

Small and portable

Low Cost:

Inexpensive to manufacture

No applicator required

Safe with No Messiness:

Minimal impact on vaginal health

Minimal to no additional vaginal discharge

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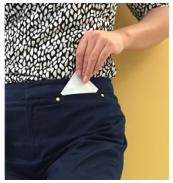
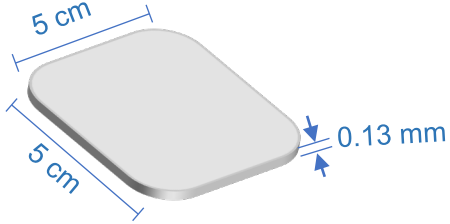
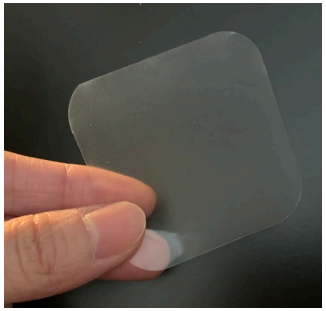
How to make vaginal films?



- **Components**
  - Drug(s)
  - Film forming polymers
  - Plasticizers
  - Solubilizers
  - Release-modifying polymers





- **Processing/manufacturing**
  - Blending/mixing – order of addition, temperature, duration, speed, deaeration, and homogenization
  - Casting – temperature, method of heating, and drying rate

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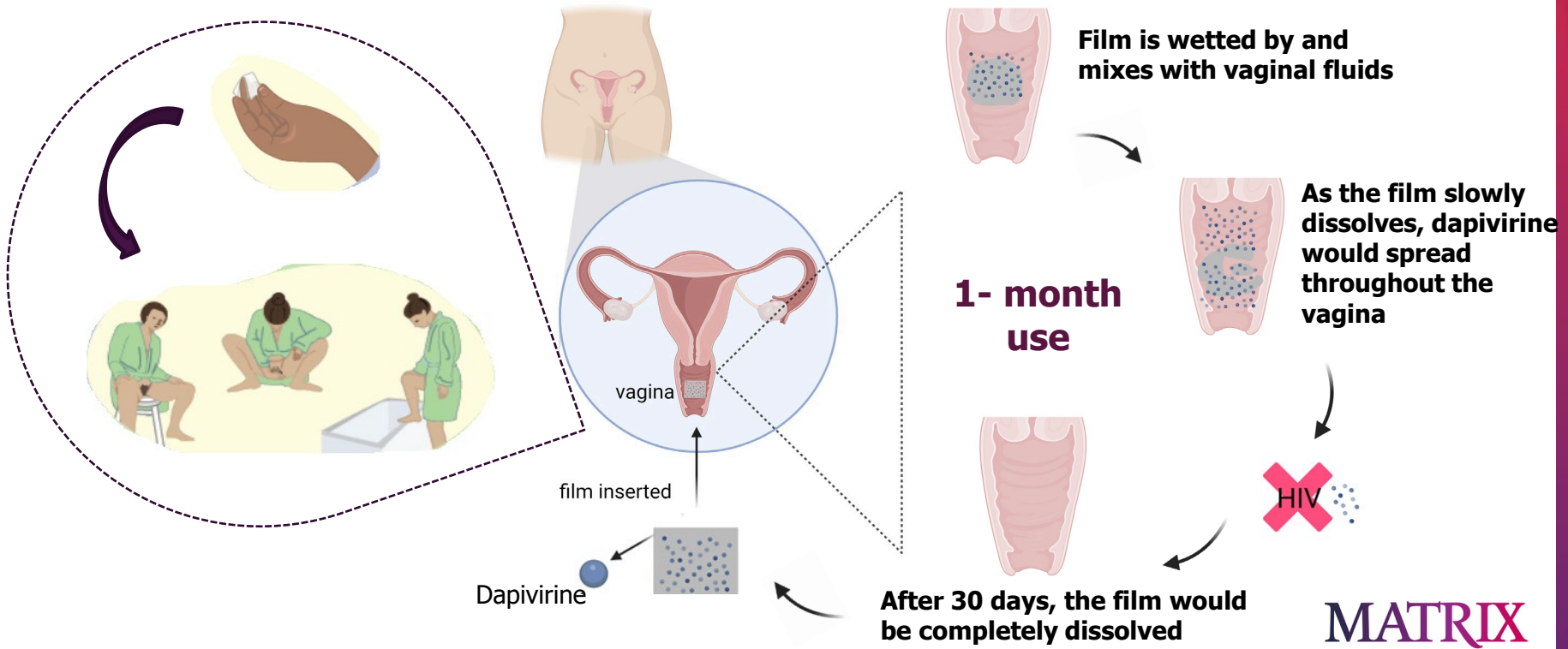
How would the film work?



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Previous experience on film development

- Dapivirine & Tenofovir quick release films (FAME-I)
  - Intended to be used at the time of sex
  - Clinical evaluation showed better drug delivery and acceptability compared to gels
  - Women expressed interest in longer duration films
- MK-2048 (anti-HIV drug) one week film (FAME-II)
  - Demonstrated safety and drug delivery in women

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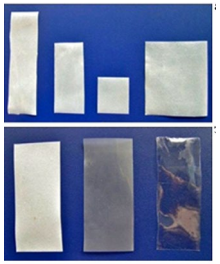
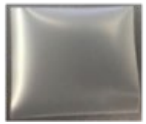
What do women think about films

PASII
526 women

Project MIST
24 couples

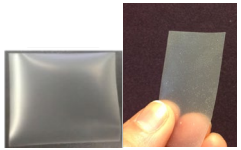


FACE
80 women



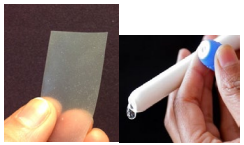
FAME-101
65 women

Films are acceptable



FLAG
32 women

FAME-04
75 women



FAME-02
60 women

>2500 women
- ✓ USA, Burkina Faso, Tanzania, Zambia, South Africa and Zimbabwe

"It's simple to use, .. it's easy, it's an easy process."

"It's not like an inconvenience if, you know. Just as simple as getting out the shower, putting it in, and then moving on. Almost like brushing your teeth."

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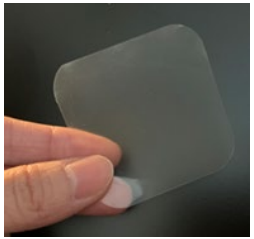
Dapivirine ring and film comparison



	DPV Monthly Ring	DPV Monthly Film
Drug loading	25 mg	34 mg
Drug release	4-5 mg DPV released in 28 days	Potentially complete drug release leading to less or no drug waste
Product removal	Required	Biodegradable; no removal necessary
Waste disposal	Required for removed rings and packaging material	Biodegradable; no product waste except packaging material
Efficacy	Overall <35% efficacy, at least partially due to adherence issues	Higher dosing level and more complete drug release may lead to higher efficacy: >50%.

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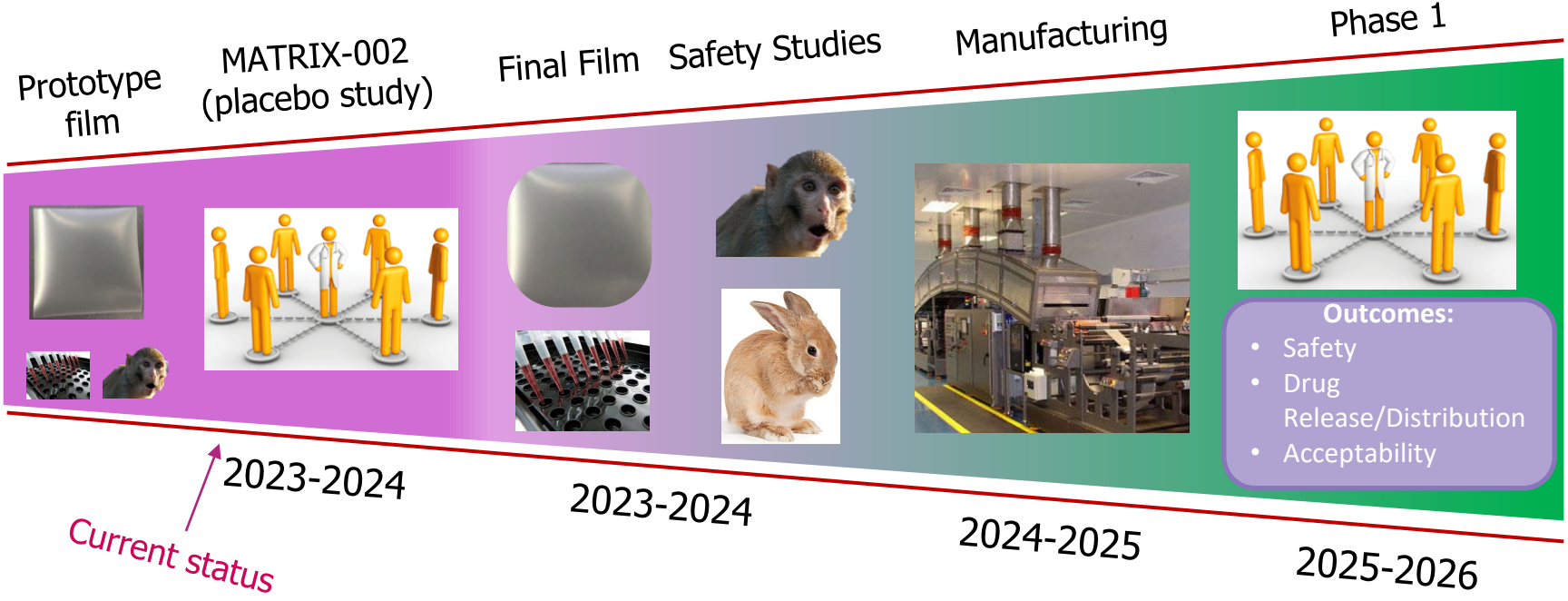
Overall product development timeline (2022-2026)

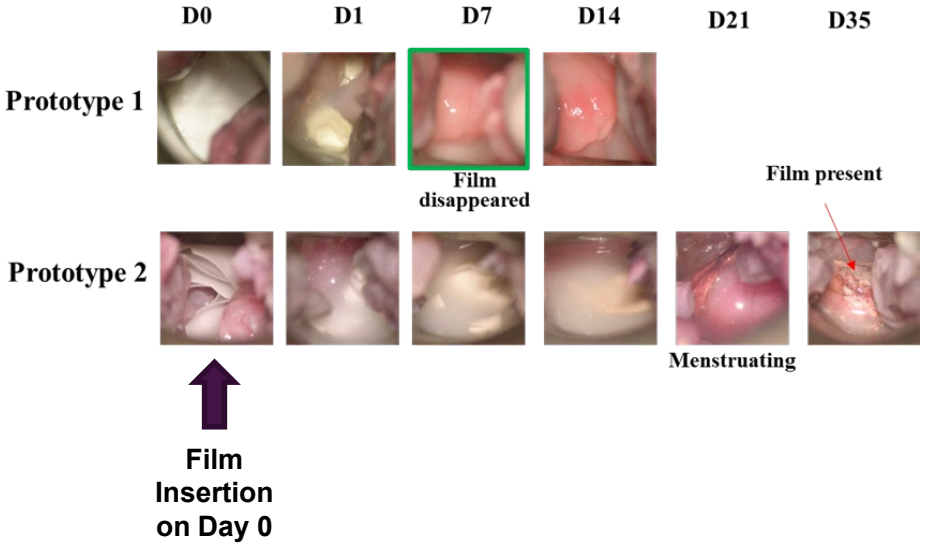


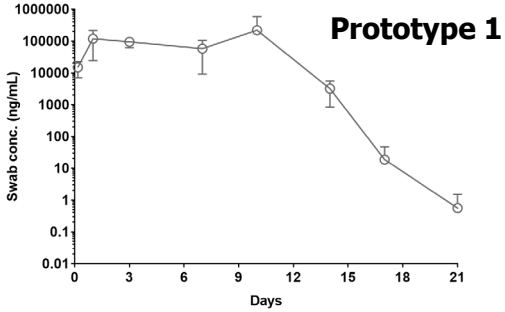
Where we are with development

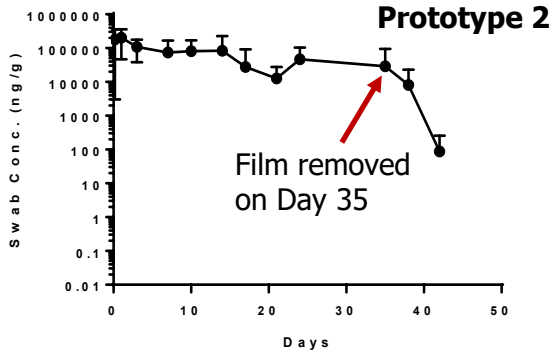
- Developed necessary methods to support dapivirine film work
- Developed multiple prototype films
- Conducted retention and pharmacokinetic studies in macaque model
- Finalized the MATRIX-002 protocol (placebo film evaluation in women)
- Modified film shape and acquired tooling to implement into MATRIX-002 trial
- Scaled and manufactured placebo product for MATRIX-002
- Initiated dapivirine film manufacturing scale up activities at our manufacturing partner
- Conducting physiological modeling for the 30-day dapivirine film product

Dapivirine film retained in macaques

Colposcope visualization of the film in the macaque vagina







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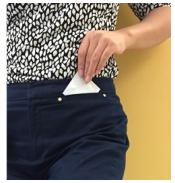
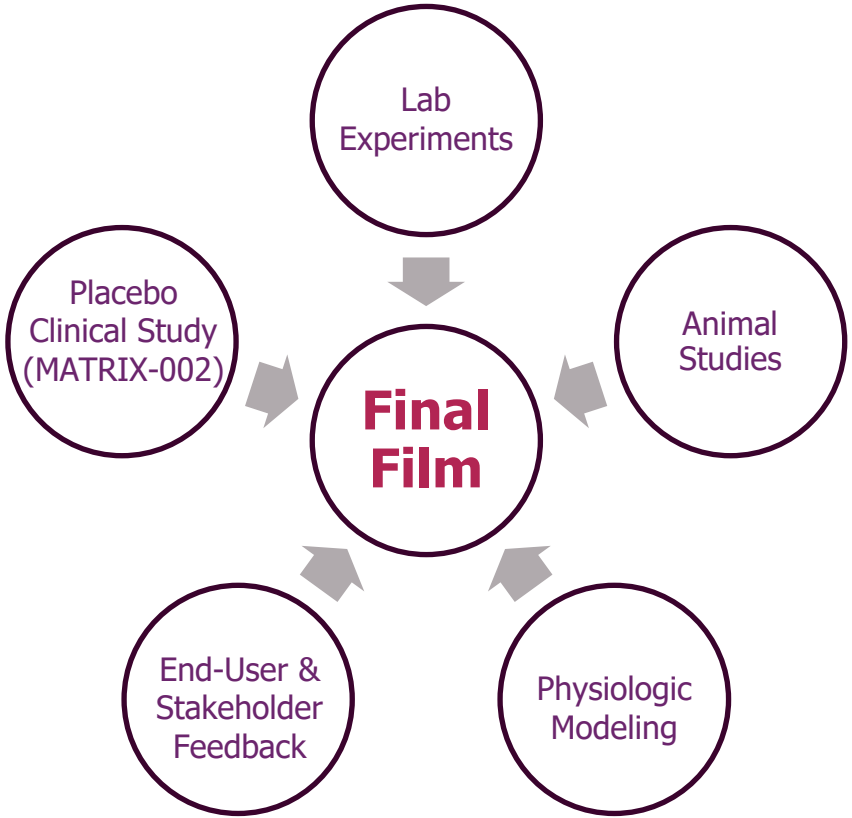
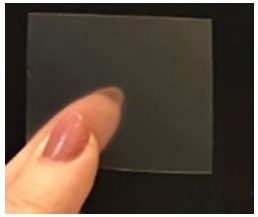
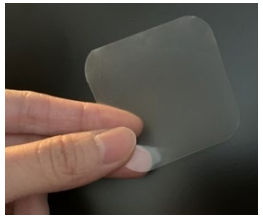
Feedback-driven development





MATRIX-002 Overview





- Trial to assess acceptability, usability and safety of two placebo prototype vaginal films which differ in shape
- To be conducted at five clinical sites (MWRI, KEMRI, Aurum, Wits RHI, HHRC)
  - 100 participants (18-45 y/o) and up to 30 sexual partners
  - Pelvic rest in 1st month, no restrictions in 2nd month
- Key questions to be addressed:
  - Do women like the vaginal film?
  - Which film shape is better?
  - Can women insert the vaginal films themselves?
  - What do sexual partners think about the film?
  - Will sex or vaginal products/practice interfere with film use?

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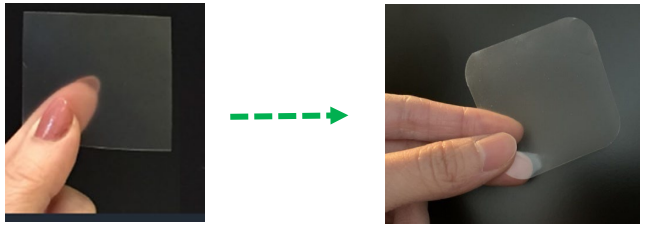
Cutting corners



Feedback from Stakeholders regarding sharp corners → Solution? → Optimal design modification: Film with rounded corners

Previous experience with film designs
Manufacturability
Minimize costs

Optimal design modification: Film with rounded corners → Procured tooling, generated prototypes → Being implemented for MATRIX-002

Final design: 3.8635 inch^2
Original Square: 4 inch^2
Waste: 4-10%+ (impact on cost)

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Next steps

- MATRIX-002 placebo study
- Dapivirine film scale up and manufacture
- Confirmatory macaque study
- Physiological modeling
- Studies supporting regulatory filing
- Phase 1 clinical study of dapivirine film

Acknowledgements

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Acknowledgements

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VALUE PROJECT TEAM

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