

Non-ARV/Non-Hormonal Dual-Purpose Monthly Vaginal Ring (Onering) (MATRIX- 003)

Developer(s)

Oak Crest Institute

Originator

<https://www.oak-crest.org/>

United States of America



The Oak Crest Institute of Science was founded in 2001 in Monrovia, California, by Dr. Marc Baum. It began as an independent, non-profit research organization with a mission to conduct impactful scientific research while training the next generation of scientists. Over the years, it has grown into a hub for interdisciplinary research, focusing on drug delivery and infectious diseases.

Sponsor(s)



U.S. Agency for International Development (USAID)

<https://www.usaid.gov/>



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

<https://www.hiv.gov/federal-response/pepfar-global-aids/pepfar>

Partnerships



Weill Cornell Medicine

<https://weill.cornell.edu/>



Wits Reproductive Health and HIV Institute, University of the Witwatersrand

<https://www.wits.ac.za/>



Contraceptive Research and Development (CONRAD)

<https://www.conrad.org/>



RTI International

<https://www.rti.org/>

Technology information

Type of technology

Intra-vaginal ring

Administration route

Topical (Vaginal)

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

Soluble adenylyl cyclase (sAC) inhibitors

Development Stage

Pre-clinical

Regulatory Approval

Not provided

Description

The dual-purpose vaginal ring is a silicone-based, doughnut-shaped vaginal ring designed for monthly contraception and prevention of diseases. It has an outer diameter of 55 mm and incorporates two drug delivery cassettes. One cassette contains a novel antiviral peptide, which is a protein fragment, while the other cassette delivers a hormone-free contraceptive agent—a soluble adenylyl cyclase (sAC) inhibitor. Both active agents are released simultaneously at a controlled rate over a 28-day period.

Technology highlight

1. Sustained Release: Enables controlled and simultaneous release of two distinct drugs within the vaginal flora, ensuring localized and prolonged therapeutic efficacy. 2. Self-Administration: Designed for ease of use, allowing users to independently insert and remove the device. 3. Cost-Effectiveness: Low manufacturing costs make it an accessible option for widespread use. 4. Extended Shelf Life: Exhibits a longer shelf life compared to other long-acting contraceptive formulations, enhancing storage stability and usability.

Technology main components

The Onering is a silicone-based, doughnut-shaped vaginal ring featuring two distinct lobes. Each lobe consists of a reservoir support structure enclosed by a rate-controlling membrane and sealed with a reservoir end cap. (i) Lobe One contains a novel antiviral peptide, which is a protein fragment. (ii) Lobe Two contains a soluble adenylyl cyclase (sAC) inhibitor.

Information on the raw materials sourcing, availability and anticipated price

Not provided

Delivery device(s)

No delivery device

APIs compatibility profile

API desired features

Small molecules

Soluble adenyl cyclase (sAC) inhibitors, including TDI-10229, LRE1, KH7, ADCY10, and TDI-11861, can be utilized in the dual-purpose design of the Onering/MATRIX-003. These inhibitors are selected for their slower dissociation rates and efficient local absorption within the vaginal environment. Currently, sAC inhibitors, whether as first- or second-line agents, have not yet received approval from any regulatory authority.

Proteins

Antiviral peptides, effective against human immunodeficiency virus (HIV), human papillomavirus (HPV), and herpes simplex virus (HSV), are targeted as a component of combination therapy in the Onering. These antivirals include (i) HIV: Enfuvirtide (T20), C34, TAT-derived peptides, VIRIP, Griffithsin; (ii) HPV: P18, L2-based peptides, HPV-16E7 peptides, RG1 epitope-derived peptides, Mimotopes; (iii) HSV: LL-37, TAT-CaM fusion peptides, BVD-21, G2 peptide, EP-100. Out of these peptides, Enfuvirtide (T20) is currently approved by USFDA (United States Food and Drug Administration).

Additional solubility data

Not provided

Additional stability data

Not provided

API loading: Maximum drug quantity to be loaded

50-75 wt%

API co-administration

2 different APIs : one API should be an antiviral peptide and other API should be a sAC inhibitor (an hormonal free contraceptive)

LogP

Not provided

Scale-up and manufacturing prospects

Scale-up prospects

Not provided

Tentative equipment list for manufacturing

Not provided

Manufacturing

Not provided

Specific analytical instrument required for characterization of formulation

Not provided

Clinical trials

MATRIX-003

Identifier

NCT06163274

Link

<https://clinicaltrials.gov/study/NCT06163274>

Phase

Pre-clinical

Status

Recruiting

Sponsor

University of Pittsburgh

More details

This research study is being conducted to find out how easy, comfortable, and safe intravaginal rings are for women to use. The two rings used in this study do not dispense any medications, are the same size, but differ in their flexibility and hardness. This study will enroll approximately 100 HIV-negative persons, aged 18-45 years, and assigned female sex at birth from sites in the United States, South Africa, and Zimbabwe. Participants will be randomly assigned to use (self-insert) Ring A for 4 weeks and then Ring B for 4 weeks or Ring B first followed by Ring A. There will be a 1-3-week rest period between using the two different rings. The study involves answering questions, undergoing pelvic examinations, and collecting blood and vaginal

fluid samples over a total of 7 in-person visit

Purpose

Trial to Assess Acceptability and Safety of Two Placebo Intravaginal Rings

Interventions

Intervention 1

Placebo Intravaginal Ring A

Intervention 2

Placebo Intravaginal Ring B

Countries

United States of America

South Africa

Zimbabwe

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2024-02-28

Anticipated Date of Last Follow-up

2024-03-21

Estimated Primary Completion Date

2024-12-01

Estimated Completion Date

2025-12-01

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations**Age Cohort**

- Adults

Genders

- Female

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: * Assigned female sex at birth. * Able and willing to provide written informed consent to be screened for and enrolled in MATRIX-003 in one of the study languages. * Able and willing to provide adequate contact/locator information. * Able and willing to comply with all protocol requirements, including: * Abstaining from other intravaginal products or practices for the duration of the study. * Abstaining from penetrative vaginal intercourse (i.e., oral-, digital-, penile-penetration) for the first 14 days of each product use period. * Refraining from participation in other research studies involving drugs, medical devices, vaginal products, or vaccines starting 2

weeks before the Screening Visit and for the duration of the study, or in observational or qualitative

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

100

Allocation

Randomized

Intervention model

Cross-over assignment

Intervention model description

Not provided

Masking

Single blind masking

Masking description

Not provided

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

Excipients

Proprietary excipients used

No proprietary excipient used

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

No novel excipient or existing excipient used

Residual solvents used

No residual solvent used

Additional features

Other features of the technology

- Drug-eluting
- Monolithic
- Removable
- Single-use
- Molded
- Reservoir-type
- At least 1 year shelf life

Release properties

Not provided

Injectability

Not applicable

Safety

The safety outcomes of the Early Phase 1 trial (MATRIX-003) have not yet been disclosed, as the study only commenced in the first quarter of 2024.

Stability

The shelf life of the formulation is longer than most of the long acting formulation i.e., 2 years.

Storage conditions and cold-chain related features

Store at a temperature range of 15°C to 30°C (59°F to 86°F).

Potential application(s)

Therapeutic area(s)

Other(s) : "HPV, HSV"

HIV

Contraception

Use case(s)

Pre-Exposure Prophylaxis (PrEP)

Treatment

Use of technology

Ease of administration

- Self-administered

Frequency of administration

Monthly

User acceptance

Not provided

Targeted user groups

Age Cohort

- Adults
- Older Adults

Genders

- Female
- Cisgender female
- Transgender female

Pregnant individuals

Unspecified

Lactating individuals

Unspecified

Healthy individuals

Unspecified

Comment

Not provided

Potential associated API(s)

Other antivirals

Class(es)

Antiviral Peptides

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

HIV, HSV and HPV

Foreseen user group

Not provided

Foreseen duration between application(s)

Once monthly

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Soluble adenyl cyclase (sAC) inhibitors

Class(es)

Hormone Free Contraceptive

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Contraception

Foreseen user group

Not provided

Foreseen duration between application(s)

Once monthly

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Patent info

There are either no relevant patents or these were not yet submitted to LAPaL

Supporting material

Publications

Miller, M., Rossetti, T., Ferreira, J., Ghanem, L., Balbach, M., Kaur, N., Levin, L. R., Buck, J., Kehr, M., Coquille, S., van den Heuvel, J., Steegborn, C., Fushimi, M., Finkin-Groner, E., Myers, R. W., Kargman, S., Liverton, N. J., Huggins, D. J., & Meinke, P. T. (2022). Design, Synthesis, and Pharmacological Evaluation of Second-Generation Soluble Adenylyl Cyclase (sAC, ADCY10) Inhibitors with Slow Dissociation Rates. *Journal of medicinal chemistry*, 65(22), 15208–15226. <https://doi.org/10.1021/acs.jmedchem.2c01133>

Soluble adenylyl cyclase (sAC: ADCY10) is an enzyme involved in intracellular signaling. Inhibition of sAC has potential therapeutic utility in a number of areas. For example, sAC is integral to successful male fertility: sAC activation is required for sperm motility and ability to undergo the acrosome reaction, two processes central to oocyte fertilization. Pharmacologic evaluation of existing sAC inhibitors for utility as on-demand, nonhormonal male contraceptives suggested that both high intrinsic potency, fast on and slow dissociation rates are essential design elements for successful male contraceptive applications. During the course of the medicinal chemistry campaign described here, we identified sAC inhibitors that fulfill these criteria and are suitable for *in vivo* evaluation of diverse sAC pharmacology.

Palanee-Phillips, T., Baum, M. M., Moss, J. A., Clark, M. R., Nuttall, J., & Romano, J. W. (2022). Drug-releasing vaginal rings for HIV/STI and pregnancy prevention: a review of recent advances and clinical applications. *Expert opinion on drug delivery*, 19(1), 47–58. [https://doi.org/10.1080/17445019.2022.2101133](#)

<https://doi.org/10.1080/17425247.2022.2020242>

Introduction: Adolescent girls and young women (AGYW), as well as pre- and post-menopausal women globally would benefit from expanded choice to address their sexual and reproductive health (SRH) needs related to Human Immunodeficiency Virus (HIV), sexually transmitted infections (STIs) and pregnancy prevention. Lack of adequate preventative vaccines for HIV/STIs reinforces public health prioritization for options women may use to mitigate risk for infectious disease and unplanned pregnancy. Drug releasing intravaginal rings (IVRs) represent one such technology that has garnered attention based on the modality's success as a pre-exposure prophylaxis (PrEP) delivery option in HIV risk reduction.

Areas covered: This article provides a synopsis of three IVR technologies in active clinical development for prevention of HIV, STI, and unintended pregnancy demonstrating advancements in terms of compatibility with a wide range of drug types with a focus on dapivirine-based silicone rings (International Partnership for Microbicides (IPM), tenofovir-based polyurethane rings (Conrad), and pod-based rings (Oak Crest Institute of Science)).

Expert opinion: The goals of IVR research are to reduce burdens of HIV/STIs and unplanned pregnancies. Through the evolution of IVR technologies, the potential exists to trigger integration of health-care services through formulation of products with multiple indications

Ridgeway, K., Montgomery, E. T., Smith, K., Torjesen, K., van der Straten, A., Achilles, S. L., & Griffin, J. B. (2022). Vaginal ring acceptability: A systematic review and meta-analysis of vaginal ring experiences from around the world. *Contraception*, 106, 16–33. <https://doi.org/10.1016/j.contraception.2021.10.001>

Objective: The vaginal ring (ring) is a female-initiated, long-acting drug delivery system for different indications, including HIV prevention. Our aim was to provide evidence for acceptability of the vaginal ring across indications to support dapivirine and multipurpose prevention technology ring introduction and roll out.

Study design: This systematic review and meta-analysis followed PRISMA guidelines. We searched PubMed, Web of Science, Embase, and grey literature for publications reporting favorable ring acceptability and secondary outcomes involving actual ring use (comfort, ease of ring use, ring comfort during sex, expulsions, and vaginal symptoms) or hypothetical acceptability for any indication published January 1, 1970-June 15, 2021. We estimated random-effects pooled prevalence, assessing between-study variation using meta-regression.

Results: Of 2,234 records, we included 123 studies with 40,434 actual and hypothetical ring users. The primary outcome assessment included 50 studies with 60 ring subgroups totaling 19,271 ring users. The favorable acceptability pooled prevalence was 85.6% (95%CI 81.3, 89.0), while hypothetical acceptability among non-ring users was 27.6% (95%CI 17.5, 40.5). In meta-regression, acceptability was higher in menopause (95.4%; 95%CI 88.4, 98.2) compared to contraceptive rings (83.7%; 95%CI 75.6, 89.5). Acceptability was lower in pharmacokinetic studies (50%; 95%CI 22.1, 77.9) compared to RCTs (89.5%; 95%CI 85.8, 92.4) and in studies assessing acceptability at ≥ 12 months (78.5%; 95%CI 66.5, 87.1) versus studies assessing acceptability at < 3 months (91.9%; 95%CI 83.7, 96.1). European (90.6%; 95%CI 83.9, 94.7), Asian (97.1%; 95%CI 92.0, 99.0), and multi-region studies (93.5%; 95%CI 84.6, 97.4) reported more favorable acceptability compared to African studies (59.4%; 95%CI 38.3, 77.5). Secondary outcomes were similarly favorable, including ring comfort (92.9%; 95%CI 89.2, 95.4), ease of use (90.9%; 95%CI 86.5, 94.0), and comfort during sex (82.7%; 95%CI 76.4, 87.6). Limitations include inconsistent outcome definitions and unmeasured factors affecting acceptability.

Conclusions: Women who used vaginal rings reported they were acceptable across indications geographic regions and indications. Policy makers should consider the ring

as an important option for pregnancy and HIV prevention drug development.

Implications: This review found favorable acceptability among vaginal ring users across indications and geographic areas, in contrast to low hypothetical acceptability among non-users. Vaginal rings are an important drug delivery system for pregnancy and HIV preventions, and scale-up should plan to address initial hesitancy among new users.

Minnis, A. M., Etima, J., Musara, P., Browne, E. N., Mutero, P., Kemigisha, D., Mgodhi, N. M., Nakabiito, C., Shapley-Quinn, M. K., Stoner, M. C. D., Hartmann, M., Macagna, N., Piper, J., & van der Straten, A. (2022). Couples' Preferences for "2 in 1" Multipurpose Prevention Technologies to Prevent Both HIV and Pregnancy: Results of a Discrete Choice Experiment in Uganda and Zimbabwe. *AIDS and behavior*, 26(12), 3848–3861. <https://doi.org/10.1007/s10461-022-03713-6>

End-user input early in biomedical product development may optimize design to support high uptake and adherence. We interviewed 400 couples (800 total participants) in Uganda and Zimbabwe to assess their preferences for multipurpose prevention technologies (MPTs) for HIV and pregnancy prevention. Using a discrete choice experiment, couples made a series of choices between hypothetical MPTs, including oral tablets and vaginal rings, inserts, and films and completed an interviewer-administered questionnaire assessing sociodemographic and behavioral measures. Most couples preferred presented MPTs over male condoms. Couples' MPT choices in both countries were influenced most by the combination of product form and dosing frequency, with monthly dosing preferred over daily. Analysis highlighted differences by country as to which side effects were most important: Ugandan couples placed greater importance on effects on the vaginal environment during sex, whereas Zimbabwean couples placed more importance on changes to menstruation and other side effects (headache, cramps). Couples' preferences signaled an openness to new

product forms and more frequent dosing if preferred characteristics of other attributes were achieved.

Additional documents

- [MATRIX-003 CLINICAL STUDY PROTOCOL](#)
- [MEDIA RELEASE](#)

Useful links

There are no additional links

Access principles

Collaborate for development



Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

Share technical information for match-making assessment



Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

Work with MPP to expand access in LMICs

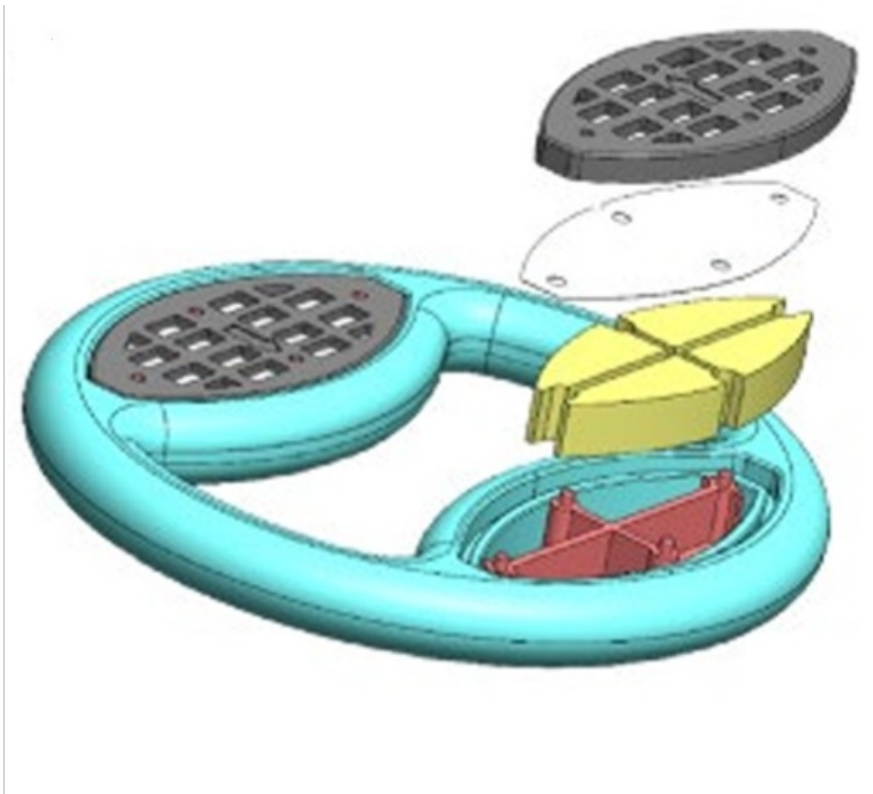


In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

Comment & Information

Illustrations



Drug-loaded Lobes of Flexible Elastomeric Vaginal Ring with multiple components for drug storage and a release member

Matrix for Prevention. (2023). MATRIX-003 Protocol Version 1.0.

https://www.matrix4prevention.org/sites/default/files/2023-10/MATRIX-003_Protocol%20Version%201.0_Final_06.29.23.pdf



Non-ARV/Non-Hormonal Dual-Purpose Monthly Vaginal Ring

Matrix for Prevention. (2024, March 20). Ring and MATRIX-003 QA.

https://www.matrix4prevention.org/sites/default/files/2024-03/Ring%20and%20MATRIX-003%20QA_%2020March2024.pdf