



Request for Applications 2023-005

Prevention Challenges: Overcoming Impediments to HIV Prevention

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Request for Applications

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I. Opportunity summary

Applicants from **United States (US), European Union (EU), United Kingdom (UK), Kenyan, South African, and Zimbabwean** institutions are invited to apply to this request for applications (RFA) sponsored by MATRIX (Microbicide R&D to Advance HIV Prevention Technologies through Responsive Innovation and eXcellence): A USAID Project to Advance the Research and Development of Innovative HIV Prevention Products for Women. The objective of this funding opportunity is to support the development of solutions to **specific challenges facing the field of HIV prevention**. Challenge solutions can stimulate the development and implementation of effective HIV prevention strategies that meet the diverse HIV prevention needs of adolescent girls and young women (AGYW), pregnant and breastfeeding women (PBFW), and female sex workers (FSWs).

Proposed applications will be composed of self-assembled groups of researchers to address challenges using one of three mechanisms. The mechanisms are:

1. **Think tanks (TTs):** groups of experts convene to provide guidance on how to address the posed challenge and propose next steps (experimental and/or logistical) to meet the challenge.
2. **Best practice working groups (BPWGs):** groups of researchers charged with identifying best practices to address a prevention challenge and, if applicable, perform limited proof-of-concept (PoC) studies to support the proposed best practice.
3. **Research challenges (RCs):** research projects where applicants propose and perform specific laboratory-based research to address the prevention challenge.

Applicants will propose activities designed to address the challenge within the RFA duration and direct cost limits. Specific challenges and their parameters are listed in Section III. TT and BPWG applicants must design applications that are based on the deliverable identified for the challenge. RC applicants will develop specific aims and conduct milestone and go/no-go driven research designed to address the scientific gap identified in the challenge. PATH, a member of the MATRIX project, will oversee application submission and award processes using an oversight structure that draws from US- and Africa-based administrators. The number of awards will be based on meritorious review of the proposals received.

Key words: HIV prevention, multipurpose prevention technology, best practices, adolescent girls and young women, antiretrovirals, microbiome, pro-inflammatory cytokines and chemokines, biobanking, delivery technologies.

II. Key dates

Table 1. Summary of key dates.

Release of request for applications	April 1, 2023 (8:00 a.m. Pacific time)
Letter of intent due	June 1, 2023 (8:00 a.m. Pacific time)
Fact-finding questions due	June 1, 2023 (8:00 a.m. Pacific time)
Applicants provided responses to fact-finding questions	June 15, 2023 (8:00 a.m. Pacific time)
Applications due	August 1, 2023 (8:00 a.m. Pacific time)
Applicants notified of decision	September 22, 2023
Estimated project start date	December 1, 2023

This RFA expires on August 2, 2023.

MATRIX reserves the right to modify this schedule as needed. Parties who express interest will be notified by email of any changes to the RFA.

III. Challenge scope and deliverables

MATRIX

The Microbicide R&D to Advance HIV Prevention Technologies through Responsive Innovation and eXcellence (MATRIX) project is designed to expedite research and development (R&D) of products for prevention of HIV in women (<https://matrix4prevention.org>). MATRIX is funded by USAID and is led by Dr. Sharon Hillier (Magee-Womens Research Institute, Pittsburgh, PA, USA) and Dr. Thesla Palanee-Phillips (University of the Witwatersrand, Johannesburg, South Africa). MATRIX's scientific and operational priorities are focused on advancing products that meet the diverse HIV prevention needs of AGYW, PBFW, and FSWs, while ensuring equitable leadership and representation of sub-Saharan African (SSA) researchers and stakeholders in all HIV prevention and multipurpose prevention technology (MPT) development activities.

Scope of work

Within the budget and time frame listed in Table 2, MATRIX is seeking a diverse pool of investigators in HIV prevention research and development, including early-stage researchers, to address the prevention challenges described in Table 3.

Approaches to the prevention challenges

Specific prevention challenges whose solutions could significantly impact the delivery of effective HIV and multipurpose prevention strategies have been identified by MATRIX and USAID. The challenges have been divided into three award mechanisms for the purpose of this RFA: think tank (TT), best practice working group (BPWG), or research challenge (RC). The specific challenges are outlined in Table 3. Responsive proposals focusing on a single challenge will be composed of a self-assembled group of researchers convened to specifically address the posed challenge. The assembled experts can be from multiple institutions across the United States, European Union, United Kingdom, Kenya, South Africa, and Zimbabwe, and each team must include one or more experts or institutions from Kenya, South Africa, and/or Zimbabwe. Expert teams can be of any size, with the size and composition commensurate with the specific challenge. The outcomes of the awards will be measured by achievement of specific deliverables for TTs and BPWGs, or milestone and go/no-go driven research outcomes for RCs. Key definitions used throughout the RFA are listed below in Section X.

Think tanks (TTs) are assemblages of experts convened to provide their best input to address a posed prevention challenge (Table 3). The objective of a TT is to define a theoretical framework that can be used to provide insight into the challenge. The deliverable for a TT is a white paper and/or formal report outlining the TT's guidance and/or findings on the topic (see Table 3). The TT challenge may be addressed by conducting stakeholder surveys, engaging subject matter consultants (5 to 10 experts), or conducting workshops or small meetings (15 to 25 attendees). A range of expertise may be required to address a prevention challenge, including but not limited to expertise in HIV (virology, immunology, and prevention) and sexually transmitted infection prevention, with involved stakeholders comprising health care providers (HCPs), potential users, regulators, and industry representatives. The TT leadership will synthesize the information generated by its deliberations and provide written recommendations to address the challenge. TT recommendations may include identifying infrastructure/administrative structures and costs needed to implement the TT recommendation. A TT may not conduct specific research to verify any aspects of their recommendations.

Best practice working groups (BPWGs) are self-assemblages of experts brought together to identify best practices for addressing a posed prevention challenge

(Table 3). BPWGs may design their best practices based on member input and/or input from external experts captured through consultations (5 to 10 experts) or a workshop or small meeting (15 to 25 experts). In contrast to TTs, the BPWG may design and/or conduct specific studies or experiments to support their best practice recommendations. BPWG recommendations may include proposing future experiments and/or developing high-quality structures and/or infrastructure supporting HIV prevention including MPT technology development using the BPWG recommendations. The final deliverable of a BPWG should be a white paper and formal report (see Table 3); if future activities for investment are identified, the BPWG should provide a costed description of the experiment and/or infrastructure as part of their final deliverables.

Research challenges (RC) will be composed of researchers and experts that will design and execute specific research to address the prevention challenge (Table 3). Applications will propose specific aims, milestones, and go/no-go activities on a timeline designed to provide information to address the challenge. RC-supported research may not result in final resolution or provide a definitive answer to the challenge; however, the results must advance knowledge on the prevention challenge, allowing additional testable hypotheses to be developed. The deliverables for an RC include a final formal report to MATRIX and USAID summarizing research outcomes plus next step recommendations and peer-reviewed manuscripts or presentations at scientific meetings to share research outcomes (see Table 3).

Table 2. Total cost limitations and duration of challenge applications.

Challenge type	Duration (up to)	Maximum total cost (US\$)
Think tanks	1 year	\$100,000
Best practice working groups	1.5 years	\$200,000
Research challenges	2 years	\$350,000 per year

Total costs may include direct and indirect costs, and if an organization has a current Negotiated Indirect Cost Rate Agreement (NICRA) with the US federal government, that rate will be approved. Organizations without a NICRA, may submit a proposal to PATH justifying an indirect cost rate that is consistently charged across all of the entity’s programs, including the PATH funded project.

The scope of the prevention challenges supported by this RFA are described in Table 3. Applicants will identify a specific challenge by its challenge number and develop an application that specifically addresses the challenge and expected deliverable. Key definitions used throughout the RFA are listed below in Section X.

Table 3. Prevention challenges.

Challenge number	Challenge title	Scope/deliverables
Think Tank (TT)		
TT-1	Determine the minimal acceptable efficacy threshold for a vaginal topical HIV prevention product.	<p>Current HIV prevention strategies using injectable or oral pre-exposure prophylaxis can result in >90% prevention of HIV infection; however, not all individuals want an oral or injectable HIV prevention method, and some women have expressed a preference for a vaginal topical HIV prevention method. Clinical studies with tenofovir and dapivirine have suggested that administration as a topical HIV prevention method can be efficacious, but end-user factors (adherence) impact the efficacy of the strategy. The objective of this TT is to define efficacy targets for vaginal topical HIV prevention product(s) that are achievable, are realistic, and reflect the input of regulatory agencies, HCPs, end users, and clinical trialists. The TT may use a variety of inputs, including modeling, to identify target efficacy thresholds. Threshold estimates should consider HCP and end-user preferences as well as contextual factors and bias that could impact adherence and uptake.</p> <p><i>Deliverables:</i></p> <ol style="list-style-type: none"> 1. A formal report with findings to MATRIX and USAID. 2. A white paper that outlines practical and achievable minimal efficacy targets for vaginal topical HIV prevention products.
TT-2	Develop a bridging structure to span the prevention drug development gap between the USAID R&D award (MATRIX) and the USAID Maximizing Options to Advance	MATRIX and MOSAIC occupy the ends of the HIV prevention drug development spectrum. However, coordination between these USAID programs is limited, with no formal bridging activities and/or infrastructure to facilitate the handoff of products completing phase 1 testing in MATRIX to later phase clinical trials, and then to MOSAIC for implementation and informed choice activities. Progressing HIV prevention including MPT products through this gap will require conducting high-

	<p>Informed Choice for HIV Prevention (MOSAIC) award.</p>	<p>quality phase II and III clinical trials to enable regulatory approval of new prevention strategies. This TT must include interactions with MATRIX and MOSAIC personnel (including leadership) to identify the administrative, operational, and oversight structure(s) required to efficiently bridge these two programs and accelerate HIV prevention product introduction. The TT should identify processes to address regulatory requirements, clinical product manufacturing, additional animal and human safety and toxicological data needs, early consideration of product implementation issues, high-quality oversight of operations and regulatory processes, and other gap-filling activities that may be required to enable bridging activities. Final recommendations should also include cost estimates to establish and maintain proposed administrative, operational, and oversight infrastructure, and the projected cost for shepherding a lead HIV prevention, including MPT products through the gap using the proposed infrastructure and administrative processes.</p> <p><i>Deliverable:</i></p> <ol style="list-style-type: none"> 1. A formal report presenting findings to MATRIX and USAID that summarizes the consultation processes used to make the TT recommendations; a costed description of the recommended administrative, operational, and oversight infrastructure required to bridge a theoretical HIV prevention, including MPT products from MATRIX to MOSAIC; and the projected costs to transition an HIV prevention including MPT product using the recommended infrastructure and processes.
<p>Best Practice Working Group (BPWG)</p>		
<p>BPWG-1</p>	<p>Develop a highly sensitive HIV prevention drug testing method for use with HIV prevention including</p>	<p>Cost-effective and accurate point-of-care detection of HIV and objective adherence monitoring in uninfected individuals is a significant barrier to deploying and implementing effective HIV prevention including MPT strategies. There are several emerging technologies that can be used to detect HIV and drugs in plasma and</p>

	<p>MPT strategies.</p>	<p>mucosal secretions. However, the development of new methods and instrumentation is costly and time consuming, so efforts must be focused on supporting the most cost-effective, accurate, and precise technology to meet this challenge. The primary objectives of this BPWG are to: (1) landscape and assess detection technologies currently under development (e.g., types, cost, health care infrastructure needed to implement); and (2) generate best practices recommendations for the selection of a lead technology and its development. Best practices should include recommendations for testing parameters/process, performance metrics, and requirements for the method to receive regulatory approval in SSA. Limited testing of detection technologies or instruments may be used to select and identify/quantify parameters central to generating best practices recommendations and identify lead technology(ies). Final recommendations should include a time and costed estimate to license the selected lead point-of-care diagnostic technology in SSA.</p> <p><i>Deliverables:</i></p> <ol style="list-style-type: none"> 1. A formal report to MATRIX and USAID that summarizes the current technology landscape; identifies the lead technology; and outlines recommended best practices to support continued development, regulatory approval, and introduction of the lead technology in SSA for clinical use as part of HIV prevention including MPT strategies. 2. A white paper published on the MATRIX website summarizing the current technology landscape and recommended best practices.
<p>BPWG-2</p>	<p>Optimize the collection of end-user perception feedback to inform prevention products.</p>	<p>Sociobehavioral research (SBR) is being increasingly employed to understand end-user and stakeholder preferences for the design/rheological properties (look, feel, etc.) and use (duration, application method, etc.) of HIV prevention including MPT strategies in development. As human-centered design has become a driving force in the development of these strategies, barriers to collection</p>

		<p>of relevant and impactful SBR data from end users have emerged. These barriers include lack of cross-study standardization of collection and analysis methods; absence of common quantifying tools to collect SBR data on look, feel, and duration; and weak processes to communicate user preferences. The goal of this BPWG is to develop best practices to optimize the collection, standardization, and communication of user SBR data and research outcomes to researchers, users, and other stakeholders across preclinical development and clinical studies (phase I, II, and II) performed in SSA. Best practices may also include the development of standardized SBR tools and data collection/analysis methods. Pilot experiments can be conducted to support proposed best practices when they include the use of specific data collection or analysis tools proposed as part of the best practice.</p> <p><i>Deliverables:</i></p> <ol style="list-style-type: none"> 1. A formal report to MATRIX and USAID that outlines best practices for collection, standardization, and communication of SBR information across clinical studies to researchers, users, and other relevant stakeholders. 2. A white paper published on the MATRIX website summarizing the recommended best practices.
BPWG-3	Optimize microbiome analysis in HIV prevention and MPT studies in low- and middle-income countries (LMICs).	The collection and analysis of microbiome samples for use in determining the impact of the bacterial microbiome on HIV acquisition and mucosal drug concentration/efficacy is complicated by several factors. Chief among these are the lack of standardized collection, handling (storage and transport), and sample processing methods. Proper sample collection, handling, and processing procedures are critical to ensure that population identification is not skewed. The goal of this BPWG is to provide best practice recommendations for the collection, handling (transport and storage of microbiome samples prior to analysis), and processing of microbiome samples. These

		<p>recommendations should lead toward optimized microbiome sample collection processes across LMIC sites performing clinical studies. Recommendations from this BPWG could also include the integration of logistic software for bacteria identification, tracking, and quality control of sampling within and across sites. Limited experimental studies to support recommended best practices for sample collection and analysis may be conducted.</p> <p><i>Deliverables:</i></p> <ol style="list-style-type: none"> 1. A formal report to MATRIX and USAID identifying the best practice recommendations to standardize microbiome sample collection, handling, and processing procedures for optimized microbiome analysis in clinical studies. Final recommendations should include a per sample cost breakdown to implement recommended best practices in a LMIC clinical setting. If the BPWG assesses costs across multiple LMIC contexts, the report should provide a cost breakdown for a representative country for each context. 2. A white paper published on the MATRIX website summarizing the recommended best practices.
BPWG-4	Establish mucosal sample biobanks in LMICs.	<p>The availability of well-curated samples (plasma, mucosal secretions, tissues, etc.) from HIV prevention technology and MPT clinical trials can be a resource for preclinical and clinical drug developers to understand clinical outcomes and develop next-generation products. Many large clinical trials in SSA have collected mucosal samples; however, access to and/or sampling intervals may not be appropriate for secondary studies, especially several years after the trial was completed. Often these samples are stored in investigator freezers without a plan for long-term stability and quality control, resulting in variable sample quality. In addition, access to samples may require extensive negotiation with multiple investigators, sites, and institutions to gain access. The</p>

		<p>goal of this BPWG is to establish a series of best practices for the collection, storage, quality control of, and access to mucosal samples used in trials conducted in LMIC settings. The BPWG would identify best practices for clinical studies for sites that currently do not have established biobanks or where a biobank could represent a unique resource for HIV and MPT researchers. The BPWG should also provide recommendations for biobank construction (storage facilities and quality assurance/logistics administration); types of samples required to provide a comprehensive and sustainable resource to users; collection methods; storage conditions; inventory monitoring systems; sample quality control; access procedures; and long-term maintenance of the biobank (five+ years). The costs for such a facility should be provided.</p> <p><i>Deliverables:</i></p> <ol style="list-style-type: none"> 1. A formal report to MATRIX and USAID outlining recommendations for the establishment, operation, and long-term maintenance of LMIC biobanks, with cost estimates (by year) for biobank establishment, access procedures, and maintenance for a minimum of five years. 2. A white paper published on the MATRIX website summarizing the recommended best practices.
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Research Challenge (RC)

RC-1	<p>Identify changes in microbiota (bacterial, viral, fungal, and phage) that impact HIV acquisition and HIV prevention product efficacy and safety.</p>	<p>The potential impacts of microbiota (particularly the bacterial microbiota) on HIV acquisition and susceptibility have been extensively studied over the last decade, with numerous studies suggesting that various microbiota (bacterial, fungal, viral, and phage) can have a significant impact on HIV susceptibility and acquisition as well as prevention drug metabolism. However, there is still significant information to be gained, especially in LMIC settings where microbiota may be more reflective of environmental influences and substantially different from</p>
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		<p>microbiota identified in non-LMIC settings. This RC will support focused research projects in Kenya, South Africa, and Zimbabwe to perform research to understand the connections between the microbiota (bacterial, viral, fungal, and/or phage) and HIV acquisition/susceptibility and prevention drug metabolism. Other studies of interest include those that: (1) elucidate the metabolic impacts of the microbiota on vaginal mucosal tissue that could influence the local immune system, drug pharmacokinetics, and pharmacodynamics; or (2) look at the impact of the microbiota on metabolome, glycome, drug transporter, and local metabolism enzymes. Applications are not required to address all potential microbiota organisms and may focus on a specific microbiota organism and its impact.</p> <p><i>Deliverables:</i></p> <ol style="list-style-type: none"> 1. Final formal report to MATRIX and USAID that summarizes the outcomes of performed studies and provides next step recommendations. 2. Peer-reviewed manuscripts and presentations at MATRIX annual meetings and other scientific meetings to disseminate results.
RC-2	Identify new drugs that could be developed for HIV prevention or incorporated into a contraceptive MPT.	<p>Although many drugs have been successfully developed and licensed for HIV prevention (tenofovir disoproxil fumarate, tenofovir alafenamide in combination with emtricitabine, dapivirine, or cabotegravir), along with numerous other approved drugs that are successful at suppressing HIV replication during treatment, there are still classes of compounds and individual drug entities that have the potential to be developed for HIV prevention or are compatible with contraceptives for pairing in MPTs. This RC explores new chemical entities of both biologic and chemical origin derived from sources in SSA. This includes synthesis of a new drug candidate and searching novel chemical sets and biosample collections from SSA for anti-HIV activity in vitro and in vivo. The proposed development may use in silico methods, medicinal</p>

		<p>chemistry processes, and prodrugging to identify/create analogs of novel chemical entities that may improve efficacy, safety, and bioavailability. Excluded from eligibility for this RC are all antiretrovirals (ARVs) currently under development, including any ARVs or non-ARVs previously reported in the literature, licensed HIV drugs and antibodies used for treatment and prevention, and searching libraries of drugs licensed for other indications for anti-HIV activity (i.e., repurposing). Specific aims and milestones should be focused on providing PoC for the new chemical entity and its efficacy in in vitro and/or in vivo studies.</p> <p><i>Deliverables:</i></p> <ol style="list-style-type: none"> 1. Final formal report to MATRIX and USAID that summarizes the outcomes of studies performed and provides next step recommendations. 2. Peer-reviewed manuscripts and presentations at MATRIX annual meetings and other scientific meetings to disseminate results.
RC-3	<p>Develop novel cost-effective method(s) for highly sensitive microbiome characterization and analyses from LMIC populations.</p>	<p>Current approaches to analyzing the microbiome in the context of HIV prevention require sophisticated and expensive equipment to identify and quantitate the bacterial species that make up the vaginal microbiome, thus restricting use of these methods to select laboratories in major research institutions. The objective of this RC is to develop new methods or approaches that can be implemented in LMIC research settings to study the vaginal microbiome of AGYW from LMICs. Method development should be aimed at elucidating identified known species of the vaginal microbiome and better methods to parse microbiome “dark matter” (currently poorly characterized bacterial species) to look for relationships to HIV susceptibility and acquisition. The RC approach may also focus on the development of more sensitive and facile analysis packages to identify and categorize dark and light matter bacterial species composing the total microbiome. A set of target</p>

		<p>specifications should be provided for the proposed methods (e.g., specificity, precision, and sensitivity).</p> <p><i>Deliverables:</i></p> <ol style="list-style-type: none"> 1. Final formal report to MATRIX and USAID that summarizes the outcomes of performed studies and provides next steps/recommendations. 2. Peer-reviewed manuscripts and presentations at MATRIX annual meetings and other scientific meetings to disseminate results.
RC-4	<p>Analyze vaginal pro-inflammatory cytokines from clinical trials in Kenya, South Africa, and Zimbabwe.</p>	<p>Multiple studies have shown that the inflammatory state of the female reproductive tract has a direct relationship to susceptibility to HIV infection. The objective of this RC is to further expand our knowledge of the role of vaginal tissue inflammation and the expression of pro-inflammatory cytokines and chemokines in the presence or absence of vaginal HIV prevention strategies as well as the relationship of these potential markers to HIV susceptibility and acquisition. This RC may not conduct clinical studies but may collect vaginal secretions from healthy volunteers with or without pre-diagnosed bacterial vaginosis. If using biobanked samples from completed or ongoing trials, proposed activities should include development and implementation of quality control processes to ensure samples used are appropriate for the proposed analysis. Inferences based on pro-inflammatory cytokine patterns on HIV acquisition and impact (positive or negative) of prevention strategies (placebo and drug containing) compared to untreated volunteers should be performed.</p> <p><i>Deliverables:</i></p> <ol style="list-style-type: none"> 1. Final formal report to MATRIX and USAID that summarizes the outcomes of performed studies and provides next step recommendations. 2. Peer-reviewed manuscripts and presentations at MATRIX annual meetings and other scientific meetings to disseminate results.

<p>RC-5</p>	<p>Detect and analyze drug-drug interactions (DDIs) between HIV active pharmaceutical ingredients, hormones, and other commonly used drugs at LMIC sites.</p>	<p>DDIs between antivirals, hormones, and other drugs (e.g., for malaria, tuberculosis, sexually transmitted infections, vaginosis, or common morbidities including heart disease and diabetes) used by people using HIV prevention strategies have been described and could constitute a significant safety and/or efficacy issue for the effective use of HIV prevention and contraceptive MPT strategies. Although some DDIs have been identified for prevention strategies and commonly used drugs in SSA, vaginal HIV prevention drugs and MPTs DDIs have yet to be thoroughly explored in LMIC contexts. The objective of this RC is to explore in vitro and in vivo (animal model) vaginal DDIs that may arise with concurrent use of HIV prevention drugs with hormones or other drugs used systemically and locally to address comorbidities that could impact vaginal prevention drug metabolism, excretion, and transport, ultimately impacting prevention strategy efficacy and safety. Studies may also be conducted to identify DDIs that occur in the female reproductive tract with use of over-the-counter vaginal products or vaginal hygiene practices used in Kenya, South Africa, and/or Zimbabwe.</p> <p><i>Deliverables:</i></p> <ol style="list-style-type: none"> 1. Final formal report to MATRIX and USAID that summarizes the outcomes of performed studies and provides next steps/recommendations. 2. Peer-reviewed manuscripts and presentations at MATRIX annual meetings and other scientific meetings to disseminate results.
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In addition to the specific deliverables cited for each activity in Table 3, prevention challenge awardees are encouraged to disseminate their findings and/or research outcomes using all available resources, including but not limited to publication of manuscripts, commentaries short communications, press releases, webinars, etc.

Nonresponsive areas of research

Applications proposing research that is identified as not responsive to this funding opportunity will be returned without review, including:

- Any proposed TT, BPWG, or RC that is not focused on or responding directly to the parameters of the prevention challenges outlined in Table 3.
- Development of any drug, product, instrumentation, or process that does not have anti-HIV activity or application to HIV prevention.
- Research that involves first-in-human, phase 1, phase 2, or phase 3 clinical trials. Applicants may propose research using samples from completed or ongoing clinical trials, but applicants may not use this RFA to support any component of a clinical trial or observational study. Applicants may propose to use tissues and/or secretions that have been specifically obtained from healthy volunteers following applicable local laws and ethics committee regulations.
- Development of new products, drugs, drug delivery systems, diagnostics, and/or technologies that do not support advancement of HIV prevention, including MPT products development.
- Any applications that propose the development of HIV vaccines (or components of vaccines), including combination of antivirals and vaccines in a single drug delivery system or as an MPT.
- Any applications with proposed innovations that are not supportive of the HIV prevention needs of AGYW, PBFW, and FSWs.
- Any applications focusing on SBR, such as end-user and marketing studies to determine general end-user perceptions, acceptability, or market interest for a specific or hypothetical HIV prevention, including MPT strategy. Applications proposing limited SBR research in support of a BPWG-2 application must design and confine the proposed SBR research to studies that provide PoC for the proposed best practice.
- Any application proposing the conduct of scientific meetings or workshops with non-MATRIX project members that are not focused on defining critical parameters to identify processes that inform the objectives of the proposed TT or BPWG deliverable. RC activities may not conduct workshops or meetings in support of their research proposal.
- RC applications where the sole role of personnel from South Africa, Kenya, and/or Zimbabwe is to provide samples for a US/EU/UK-based RC activity.

Deliverables

- Specific deliverables for each prevention challenge are described in Table 3.
- Each project team will need to complete a risk register following the first month of the project. A template will be provided upon acceptance of an application.

- Each project team will need to complete a one-page report every six months to update PATH on the project status. A template will be provided upon acceptance of an application.
- At the end of the award period, each project team will need to present project results to the MATRIX steering committee and USAID. Each team will also provide a summary of the project results along with any publications for posting on the MATRIX website. Confidential information may be excluded from the results presentation and/or from the MATRIX website, as appropriate.
- At the discretion of MATRIX leadership and USAID, the team may be asked to provide formal updates on progress and results.

IV. Award information

MATRIX expects the following:

- **Number of awards:** The number of awards will be based on the meritorious review of the submitted proposals. The total number of awards is contingent upon the number and topic of submissions, available funds, and the applications' applicability to MATRIX's mission and objectives. MATRIX reserves the right to fund multiple awards for a specific challenge and manage them in concert to address the challenge.
- **Award budget:** Budget limitations are described in Table 2. Budgets should be detailed, reasonable, and realistic.
- **Award project period:** The duration of each challenge type is described in Table 2. A single no-cost extension up to an additional six months may be requested. Requests must be submitted formally two months prior to the end date of the award. However, MATRIX reserves the right to deny the request for any reason.

V. Eligibility information

- The proposed research needs to **address a single, specific prevention challenge** using the identified mechanism in Table 3 to support the goals and objectives of the MATRIX project and USAID.
- **Applicants from US, EU, UK, Kenyan, South African, or Zimbabwean institutions** (e.g., universities; private, for-profit, or not-for-profit small companies; university researchers and research consortia/programs; and innovation or incubation hubs) consisting of students, postdoctoral fellows, and new/early and

established investigators are invited to apply. Foreign nationals from Kenya, South Africa, or Zimbabwe working in the US, EU, and UK are eligible to apply.

- Project applications must involve significant participation and/or leadership from Kenyan, South African, and/or Zimbabwean investigators. For TT and BPWG, the application must be either led or co-led by a representative from Kenya, South Africa, or Zimbabwe. For RC, the leadership and the research teams should contain appropriate representation from one or more of these three countries. Inclusion of personnel from these countries whose sole role is to provide samples for a US/EU/UK-based RC activity does not constitute representation on the research team.
- Principal investigators (PIs) must have the skills, knowledge, and institutional resources necessary to support the generation of the requested outcomes for TT and BPWG, or if an RC, carry out the proposed research.
- Projects that would use funds to provide material support or resources to individuals, entities, or organizations of countries that have been identified by the United States Department of State as state sponsors of terrorism are ineligible. The countries currently identified are Cuba, Iran, North Korea, and Syria.
- Project applications can be submitted by USAID award holders, including MATRIX's existing partners.
- Applicant organizations or PIs may submit applications to multiple prevention challenge topics, provided that each application does not overlap with and is scientifically distinct from other submitted applications.

VI. How to respond to this request for application

During the application and award processes, operational and research oversight for this funding opportunity will be provided by PATH (www.path.org), a member of the MATRIX project. PATH will provide guidance on the RFA application submission process and budgeting should questions arise prior to the award. Applicants should submit a letter of intent to PATH via email to MatrixTechAcceleratorRFA@path.org. Applicants may submit questions via the same email; questions and answers will be sent to all those who express interest. Following submission, applications will be screened for responsiveness to this RFA. PATH will manage the review using procedures designed to minimize conflicts of interest and ensure confidentiality of the applications. The review committee will be cochaired by PATH personnel from the United States and sub-Saharan Africa, and the review committee will be composed of internal MATRIX and external subject matter experts. After the award, PATH will appoint a technical liaison to assist the awardee in management of the award.

Step 1. Letter of intent

By the date listed in Section II of this document, prospective applicants must submit a letter of intent that includes the following information:

- Identification of the prevention challenge (number [e.g., RC-4] and title) to be addressed by the application.
- Descriptive title of proposed activity.
- Name(s), address(es), and telephone number(s) of the PI(s).
- Names of other key personnel.
- Participating organization(s).
- Number and title of this funding opportunity.
- Names of suggested reviewers or people who should not review the application due to potential conflict of interest.

The letter of intent should be sent via email to MatrixTechAcceleratorRFA@path.org.

If a PI intends to submit multiple applications, a separate letter of intent should be sent for each application. Each letter of intent must not overlap with, and should be scientifically distinct from, other submitted letters of intent.

The subject line of the email should read as *RFA2023-005_letter of intent_organization_Pi Name*. For example, an application from PATH would read as *RFA2023-005_letter of intent_PATH_J Doe*.

Step 2. Fact-finding questions

Questions concerning this opportunity are welcome. The questions and answers will be provided to all participants who confirm interest. See Section II of this document for related dates. Questions received after the due date may not be accommodated. At its discretion, MATRIX reserves the right to have additional rounds of fact-finding questions, which would be sent out to all participants who confirm interest.

The fact-finding questions should be sent via email to MatrixTechAcceleratorRFA@path.org.

The subject line of the email should read as *RFA2023-005_Organization_fact-finding questions*. For example, an application from PATH would read as *RFA2023-005_PATH_fact-finding questions*.

Step 3. Applications

Completed applications should be submitted via email to MatrixTechAcceleratorRFA@path.org.

The subject line of the email should read as *RFA2023-005_application_Organization_Pi Name*. For example, an application from PATH would read as *RFA2023-005_application_PATH_J Doe*.

Formatting requirements

Applications that do not follow the requirements below will be returned without review.

- Applications must be in English.
- Budgets must be in US dollars.
- The technical application and budget narrative must be written in 11-point font or larger in a standard font (e.g., Arial, Calibri, Times New Roman). Their pages should be on US letter-sized paper (8.5 x 11 inches or 22 x 28 cm) with 1-inch margins (2.54 cm). Pages should be numbered using an X of Y format in the lower left-hand corner (e.g., 3 of 5).
- Biographical sketches, or biosketches, should follow the United States National Institutes of Health biosketch requirements, without the “Contributions to Science” section (<https://grants.nih.gov/grants/forms/biosketch.htm>). An eRA Commons account is not required for application.
- Tables and charts can be in 10-point font and must be readable without magnification.
- The detailed budget must be submitted in an Excel file, and all other files must be submitted as PDF files. Do not send locked or password-protected files.
- If confidential data or information is contained in the application, the phrase “Confidential—do not disseminate” should be placed in the footer of each page that contains confidential information.
- Each submitted document should follow the naming convention: *RFA2023-005_file name_Pi name*.

Application components

Your submission should include the following four attachments:

1. **Technical application (use the template provided):** A template for the technical application is attached to this RFA. The template also will be sent to all applicants who express interest. Label this file *RFA2023-005_technical application_Pi name*. The technical application should describe how your project addresses the objectives of the RFA and how you would work with MATRIX and its partners to achieve the deliverables. See Section VII of this document for detailed technical application requirements.
2. **Biosketches (for relevant personnel only; no page limit):** Label this file *RFA2023-005_biosketches_Pi name*. The suggested format is a US National

Institutes of Health biosketch, without the “Contributions to Science” section (<https://grants.nih.gov/grants/forms/biosketch.htm>). An eRA Commons account is not required for this application.

3. **Detailed budget (use the template provided; no page limit):** See Section VIII of this document for detailed budget requirements. The detailed budget template is attached to this RFA; it also will be sent to all applicants who express interest. Label this file *RFA2023-005_detailed budget_PI name*.
4. **Budget narrative (use the template provided; no page limit):** The budget narrative should describe how you arrive at your total dollar amount in each line item of your detailed budget. It should also provide justifications for each proposed budget item. See Section VIII of this document for detailed budget narrative requirements. The budget narrative template is attached to this RFA; it also will be sent to all applicants who express interest. Label this file *RFA2023-005_budget narrative_PI name*.

Step 4. Conclusion of process

Applicants will be notified of MATRIX and USAID’s decision by the date listed in Section II of this document. See Section IX of this document for the review criteria that will be used to evaluate submissions. Final awards are subject to the terms and conditions included in this solicitation, as well as successful final negotiations of all applicable terms and conditions affecting this work.

Unsuccessful applicants will receive feedback from the review panel. Applicants are welcome to modify their applications and submit a new application in future rounds of the RFA.

VII. Application requirements—technical

The technical application should be no more than seven pages (technical narrative: six pages; timeline: one page) and follow the template provided. Include a narrative on your technical approach to accomplish the scope of work and deliverables per Section III of this document, including:

- PI details: Name, job title, organization, department, country, email address.
- Identification of the prevention challenge (number [e.g., RC-4] and title) to be addressed by the application.
- Project overview.
- Discussion of project management and roles of the project team.
- Significance and innovation of the proposed work.
- Description of technical approach to the prevention challenge.

- Anticipated problems and solutions.
- A brief discussion of major internal and external resources, including facilities and essential equipment available to support the proposed research in this application.
- Timeline to meet the deliverables. The timeline should not exceed one (single) page and include appropriate milestones and go/no-go criteria.

Information gathering for TT and BPWG applications

In addition to the members of the TT or BPWG, the application can propose information gathering activities. These information gathering activities can take the form of a consultation (5 to 10 invited experts), a workshop or small meeting (15 to 25 experts), or a survey directed toward a specific target group, (e.g., end users, HCPs, or other stakeholders). If a consultation, workshop, or small meeting is proposed, the application must identify the specific cost, number of attendees, and types of experts to be invited as well as provide a draft agenda.

Timeline to meet the deliverables

All TT and BPWG applications must provide detailed timelines on how they will achieve the specific deliverable identified in Table 3. The creation and development of the deliverable by the funded activity must be governed by a timeline or Gantt chart with appropriate milestones and go/no-go criteria used as measures of progress toward the deliverable.

RC applications should include specific aims with a supporting timeline/Gantt chart that specifies milestones and go/no-go criteria that allows measurement of research progress.

For all applications, it is preferred that the timeline is depicted as a graphical representation (e.g., Gantt chart), although timelines in a table format are also acceptable. The timeline, milestones, and go/no-go criteria should be listed together on a single page. Milestone(s) and go/no-go criteria should not restate specific aims or deliverables; rather, they should be composed of independent descriptive statements that quantify the success or failure of the research. Examples of milestones and go/no-go criteria are included in the technical application template.

VIII. Application requirements—financial

Detailed budget (use template provided)

Budgets must be in US dollars.

Budgets must list itemized costs for the total scope of the project based on the scope of work and deliverables outlined in Section III of this document. The final scope of work may be subject to negotiation. However, application selection will be made based on the original scope of work.

The budget template provides more instructions and separates costs into the cost categories outlined below.

Personnel—inclusive of salary and leave

- Salary rates of key staff.
- Total number of days in the budget for each staff member.

Fringe benefits

- Costs associated with benefits.

Travel

- Transportation and per diem costs (other travel-related costs, such as vaccines and passports, should be listed in the “Other direct costs” section). For RCs, travel is limited to one scientific meeting annually plus well-justified travel necessary for coordination among collaborators.
- TT and BPWG applications may include costs for obtaining input from external experts using consultations (5 to 10 individuals) and/or conducting a workshop and/or small meeting (15 to 25 attendees). Describe the costs associated with the proposed consultation, workshop, or meeting, including any proposed support for attendee travel.

Equipment

- Equipment is defined as an item costing US\$5,000 or more and having a useful life of more than one year. Note: At USAID’s discretion, equipment may need to be returned at the end of the awarding period.
- Requests for new equipment should not exceed 10 percent of the total budget. A strong justification must be provided for any equipment purchase. Any application requesting an equipment budget greater than 10 percent must receive prior approval.
- Electronic equipment—such as computers, tablets, and smartphones—must be well justified for the proposed work. They should be listed as a separate line item in the budget.

Supplies

- Supplies required to perform the scope of work that do not meet the definition of equipment (i.e., cost less than US\$5,000 or have a useful life of less than one year).
- Animal acquisition and handling costs must be kept as separate line items.

Contractual costs

- Consultants.
- Subagreements.
- Subcontractors.

Construction—not applicable for this scope of work

- Applications with requests for costs to construct or modify research spaces to conduct the proposed work will be returned without review.

Other direct costs

- Itemization of all other direct costs that do not fall under the categories above.
- Include costs associated with hosting any proposed consultations, workshops, or meetings, such as renting of a meeting room, audio/visual equipment rental, etc.
- Non-allowable direct costs include construction of, or modifications to, research spaces; rent; general office equipment; and transportation costs not associated with described travel. Applications with such requests will be returned without review.

Indirect costs

- Organizations with a Negotiated Indirect Cost Rate Agreement (NICRA) with the US government may use that rate.
- Organizations that do not have a NICRA may submit an application to PATH justifying an indirect cost rate that will be consistently charged across all of the entity's programs.
- If an indirect cost rate is budgeted, a NICRA or other supporting documentation that outlines a cost allocation policy and methodology must be provided.

Total project costs

- State the total project costs as well as Year 1 and Year 2 budgets.

Cost share

USAID requires a 5% cost sharing for all awards. Awards will not be made without a commitment by your institution or partners for cost sharing. Cost sharing can come from

various sources, including but not limited to, volunteer services, donated employee time, donated supplies, cash contributions, donated equipment, or project co-funding. Resources must come from non-US government funds; NIH and USAID grants cannot be used to meet the cost sharing requirement. The cost share requirement can be met throughout the life of the award. In the template for budget narrative, describe how your project will meet the cost sharing requirements and reflect the cost share amount in the detailed budget.

Please refer to [2 CFR 200.306](#) for additional information.

Budget narrative (no page limit, use template provided)

The budget narrative should follow the layout of the detailed budget and describe how you arrived at the total dollar amount for each line item of your detailed budget.

IX. Review criteria

The following is a list of significant criteria against which applications will be assessed:

- Significance and innovation
 - Does the proposed research have the potential to have a significant impact on the field's understanding and resolution of the prevention challenge it is in response to?
 - Does the proposed research develop an original and innovative approach, process, or technology to inform the prevention challenge? Note, the proposed activity for TT and BPWG projects must focus on the challenge and be designed to deliver the stated award deliverables (Table 3). Innovation is not a major driving factor for a proposed TT or BPWG project. RC projects must be original, innovative, and address the described prevention challenge.
- Approach
 - Are the proposed approaches, study designs, methods, and analyses adequately described and realistic for the time frame of the award?
 - Does the application include appropriate time-bound milestones and go/no-go criteria?
 - Are the timeline and budget appropriate and realistic for the proposed project?
 - Will the generated data support the proposed outcomes and go/no-go criteria and provide new insights that inform or resolve the prevention challenge?

- If the TT or BPWG proposes engaging consultants, conducting a workshop, or having a small meeting to assist in developing the required deliverables: (a) Are these activities adequately described? (b) Will the proposed attendees and agenda achieve the stated goal of the consultation, workshop, or meeting? And, (c) is conducting the consultation, workshop, or meeting critical to the success of the challenge proposal?
- PI's qualifications and research environment
 - Does the PI possess the proper training and experience to direct and/or manage the proposed challenge?
 - Does the proposed team have the expertise to address the proposed challenge?
 - For TT or BPWG challenges, are all the team members required and is all required expertise needed to address the applicant's proposed activities represented?
 - Are the proposed facilities to support the prevention challenge adequate for the proposed applications? Does the team have access to specialized instrumentation or facilities required to address the prevention challenge?

MATRIX reserves the right to include additional criteria.

X. Key definitions

The following definitions are used for key terms throughout this document:

- **Deliverables:** These are the specified outputs for each challenge. The deliverables for each challenge are listed in Table 3 and should describe the outcomes of the funding (e.g., summarizing best practices, describing administrative or infrastructures required or built, and future costing). In addition to the specific deliverables cited for each activity in Table 3, prevention challenge awardees are encouraged to disseminate their findings and/or research outcomes using all available resources, including but not limited to publication of manuscripts, commentaries short communications, press releases, webinars, etc.
- **Formal report:** A report submitted to MATRIX and USAID summarizing the outcomes of the challenge award and the features of the solution that was developed in response to the prevention challenge's objectives. It may provide specific plans and/or descriptions of administrative and/or research structures needed to support the proposed recommendations.
- **White paper:** An informational document communicated by the awardee to MATRIX. The white paper may be published on the MATRIX website and/or in a peer-reviewed journal. It highlights/describes the features of the solution that was

developed in response to the objectives of the funding topic. It may provide specific plans and/or descriptions of administrative and/or research structures needed to support the proposed recommendations.

- **Proof of concept (PoC):** Evidence, generated through experimental methods, that a concept meets preestablished criteria.
- **Multipurpose prevention technology (MPT):** The combination of drugs delivered through a single drug-delivery system to provide combined protection against at least two sexual and reproductive health risks, such as unintended pregnancy, HIV, and other sexually transmitted infections.
- **Milestone:** A milestone is a measure of progress. Milestones identify critical junctures/steps in the research process that must be accomplished/completed to successfully complete the proposed research. A milestone may also incorporate go/no-go criteria in its description as measures of progress in attaining the milestone.
- **Go/no-go criteria:** These are critical decision points stated as absolutes in the timeline. Go and no-go statements/criteria are an integral part of defining a milestone. Go is a decision to continue development. No-go is a decision to stop development or modify the research activities. A single milestone may have multiple go/no-go criteria, depending upon its complexity. A go decision allows the research program to proceed to the next milestone.

XI. Terms and conditions of the solicitation

Notice of nonbinding solicitation

MATRIX and PATH reserve the right to reject any and all applications received in response to this solicitation. MATRIX and PATH are in no way bound to accept any application.

Confidentiality

All information provided to MATRIX and PATH by the applicant as part of this solicitation will be treated as confidential. If any information is inappropriately released, MATRIX and PATH will seek appropriate remedies as allowed. With the fact-finding questions as an exception, all letters of interest, applications, discussions, and information received in response to this solicitation will be held as strictly confidential within the MATRIX project and its partners, except as otherwise noted.

Conflict of interest disclosure

Applicants must disclose any actual or potential conflicts of interest (Col) via email to MatrixTechAcceleratorRFA@path.org. Col could be present if there is a personal relationship with a MATRIX and/or PATH staff member that constitutes a significant financial interest, board memberships, other employment, and ownership or rights in intellectual property that may be in conflict with the applicant's obligations to MATRIX and/or PATH. When necessary, a management plan that provides mitigation of potential risks presented by the disclosed conflict of interest will be created. Not reporting any Cols via email indicates that no Cols are present. Failure to disclose any actual or potential Cols will result in the application returned without review.

Communication during application process

All communications regarding this solicitation shall be directed to MatrixTechAcceleratorRFA@path.org. Contacting third parties that are not part of the research team but are involved in MATRIX or operations of the technology accelerator, the review panel, or any other party may be considered a Col and could result in disqualification of the application.

Acceptance

Acceptance of an application for evaluation/review does not imply funding of the application as submitted, nor does it imply acceptance of its terms and conditions. MATRIX and PATH reserve the right to negotiate on the final terms and conditions of the award. MATRIX and PATH additionally reserve the right to modify the substance of the finalist's application, such as milestones and go/no-go criteria, as well as the option to accept partial components of an application, if appropriate.

Third-party limitations

MATRIX and PATH do not represent, warrant, or act as an agent for any third party as a result of this solicitation. This solicitation does not authorize any third party to bind or commit MATRIX and PATH in any way without our express written consent.

Application validity

Applications submitted under this request shall be valid for 90 days from the date the application is due.

Intellectual property

Intellectual property generated under this award will be owned by awardees who are nonfederal entities. USAID can access the intellectual property and may authorize it for US federal purposes.

Conflict resolution

The PI is responsible for conducting the research in accordance with the agreed upon scope of work. Additionally, it is the responsibility of the PI to manage research collaborations and any conflicts that arise within the proposed research team.

Throughout the award period, project teams are expected to meet with an assigned technical liaison to track progress and risks. Any disagreements that may arise in scientific or programmatic matters (within the scope of the award), any missed milestones, or no-go decisions reached will necessitate a meeting with the technical liaison, Technology Accelerator Domain 1 cochairs, and the MATRIX leadership to discuss the future of the project. MATRIX leadership will make the final decision on how the project will proceed.

Terms and conditions of the award

USAID, the federal awarding agency for this award, specifies requirements to be placed on all funded research. These terms and conditions are non-negotiable upon acceptance of the award. Applicable links to 2 CFR 200, 2 CFR 700, and Standard Provisions are included below as a reference.

- 2 CFR 200, applies to US- and non-US-based organizations: <https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200?toc=1>
- 2 CFR 700, applies to US- and non-US-based organizations: <https://www.ecfr.gov/current/title-2/subtitle-B/chapter-VII/part-700>
- Mandatory Standard Provisions for US-based organizations: <https://www.usaid.gov/ads/policy/300/303maa>
- Mandatory Standard Provisions for non-US-based organizations: <https://www.usaid.gov/ads/policy/300/303mab>
- Additional Mandatory Standard Provisions for fixed amount awards for US- and non-US-based organizations: <https://www.usaid.gov/ads/policy/300/303mat>