Scientific Advisory Group Charter

For

Microbicide R&D to Advance HIV Prevention Technologies through Responsive Innovation and eXcellence (MATRIX)

USAID Cooperative Agreement # 7200AA22CA00002

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Abbreviations

AGYW: Adolescent girls and young women pregnant
API: Active Pharmaceutical Ingredient
ARV: Anti-retroviral
BC: Market strategy and Business Case
CMC: Chemistry, Manufacturing, and Control
CP: Critical PATH
EST: Eastern Standard Time for the United States of America
FSW: Female Sex Workers
FIH: First in Human clinical trial
GLP: Good Laboratory Practices
GMP: Good Manufacturing Practices
HCD: Human Centered Design
HIV: Human Immunodeficiency virus 1
IDE: Investigational Device Exception
IND: Investigational Drug Application
MATRIX: Microbicide R&D to Advance HIV Prevention Technologies through Responsive Innovation and eXcellence
MBR: Milestone and Benchmark Report
MWRI: Magee-Womens Research Institute
MOP: Manual of Operations for MATRIX
MPT: Multipurpose Prevention Technologies
NDA: New Drug Application
NDE: New Device Application
PDL- Product Development Leader
PI: Project Investigator
POC: Point of Contact
PRIME: Leadership of MATRIX, (Drs. Hillier and Palanee-Phillips)
R&D: Research and Development
SAG: Scientific Advisory Group for MATRIX
SBR: Socio-behavioral research
SRB: Sexual and reproductive health
SC: Steering Committee of MATRIX
SSA: Sub-Saharan Africa
USA: United States of America
USAID: United States Agency for International Development
PBFW Young women pregnant and breastfeeding women

Background

The Microbicide R&D to Advance HIV Prevention Technologies through Responsive Innovation and eXcellence (MATRIX) Collaborative is designed to expedite research and development (R&D) of products for prevention of HIV in women. MATRIX is funded by United States Agency for International Development (USAID, Awarded December 1, 2021) and is led by Dr. Sharon Hillier (Magee-Womens Research Institute (MWRI), Pittsburgh PA, USA) and Dr. Thesla Palanee-Phillips (University of the Witwatersrand Johannesburg, South Africa). Through a co-creation process with USAID and under their leadership the collaborative is composed of a wide range of inter-disciplinary partners with product Research and Development (R&D-related experience in women-initiated anti-human immunodeficiency virus-1 (HIV) -based prevention methods, including expertise in developing a range of antiretroviral (ARV)-based prevention modalities; drug formulation and delivery; long-acting, topical and systemic drug delivery; sexual and reproductive health (SRH), HIV prevention product development; socio-behavioral research (SBR) as well as market strategy and Business Case (BC) assessments and capacity strengthening. MATRIX is designed to be a dynamic and adaptable award with emphasis on actively managing projects through a "stage gating" process to remain time and resource efficient (e.g., timely discontinuation of activities that are no longer of the highest priority or projects which have met roadblocks threatening their feasibility). Stage-gating is defined as a time-based milestone-driven decision-making process that establishes Go/No-Go and achievement benchmarks for each product at defined development stages. MATRIX may also on-ramp new products judged to be of scientific priority to MATRIX to fill known gaps in biomedical HIV prevention. All R&D, SBR, clinical trial, and BC development within MATRIX are interconnected, with a priority focus on ensuring equitable leadership and representation by Sub-Saharan Africa (SSA) stakeholders, to advance products that meet the diverse HIV-prevention needs of adolescent girls and young women (AGYW), pregnant and breastfeeding women (PBFW), and female sex workers (FSW).

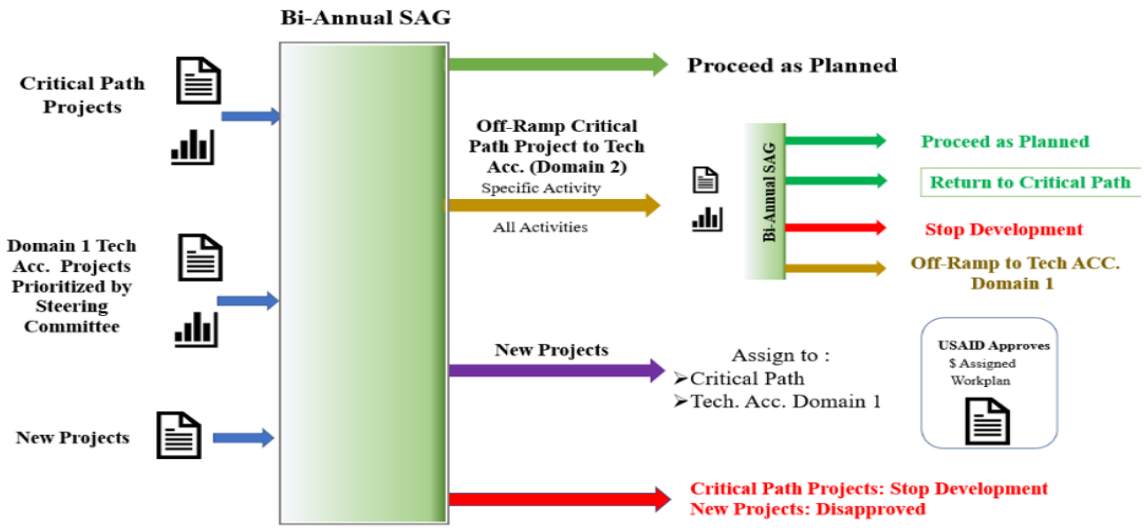
Scientific Advisory Group (SAG)

Critical to ensuring active curation of MATRIX's portfolio of products is the SAG. The SAG is an external, neutral, cross-cutting, multidisciplinary committee that will provide expert data review and consultation services to inform the MATRIX stage-gating process. Furthermore, the SAG will also provide expert advice to MATRIX product developers, end-user researchers, market/business teams, and the Technology Accelerator groups. Biannually the SAG will provide an independent unbiased assessment of progress for MATRIX product development efforts. The SAG will be the primary evaluation body for assessing progress of CP products and Technology Accelerator activities (Domain 1 and 2.) using the stage-gating process (see Figure 1). The SAG will also evaluate mitigation plans used to report development problems and, in some cases, recommend off-ramping of CP products to the Technology Accelerator Domain 2 for problem mitigation. The SAG will also make recommendations of futility determinations (stopping development) for CP, and Domain 1 and 2 Technology Accelerator activities.

The SAG is solely an evaluation and recommendation committee for MATRIX supported activities. All final decisions impacting the products (CP) and "game-changing" research

(Technology Accelerator) programs supported by MATRIX, are approved by USAID and implemented by MATRIX.

Figure 1: MATRIX Stage-Gating Process



The SAG will be chaired by a USAID approved non-voting and non-conflicted representative of the PRIME. SAG membership (personnel and committee size) may vary as the portfolio of products advance and/or stage-gating eliminates or modifies the status of products within the MATRIX development environment. An alternative SAG chair will be appointed and approved by USAID and assume the SAG chairs duties when the primary SAG Chair is unavailable.

SAG outcomes will be used to measure the success or failure of HIV prevention and Multipurpose Prevention Technologies (MPT) products being developed by MATRIX. Measurement will be in the form of a considered evaluation of individual drug development efforts by evaluating progress on timelines, milestones, benchmarks, and Go-No-Go criteria at each meeting. Success is defined as achieving the proposed timelines, milestones, benchmarks, and Go-No-Go criteria (measures) for each product being developed. Although these measures vary from product to product and are based on their current state of development, all measure guided R&D efforts are ultimately focused on submitting a pre-IND and/or enabling clinical testing of the products within the duration of the MATRIX award.

Overview of the SAG Evaluation Process

Appendix 1 contains an overview of the 60-day SAG review evaluation cycle. The cycle starts with receipt of the MBR, Mitigation Plan, or New Project Request (Appendices 4-6) 30 days prior to the SAG meeting from each project. During the interval between the receipt of plans and the SAG meeting, the plans are read, completeness determined, and sent to USAID, SAG and PRIME for reading. Triage reviews (see below) identified, approved by USAID and communicated to the appropriate product development leader (PDL). Ten (10) days before the SAG meeting meets, the SAG Chair communicates with the PDLs to identify any essential MBR updates and specific

questions to pose to the SAG, and any supplemental information distributed to the SAG 3 days prior to the meeting. During this time, it can be determined if a pre-call with the SAG is required to facilitate the meeting. On day 0 the SAG meeting is conducted. The results (SAG final recommendations) are communicated to the PRIME and USAID on day +1 and by day +7 USAID will approve or disapprove the SAG recommendations. The PDLs will then be informed of the USAID approved final recommendations by day +10 to +15. Between the end of the meeting and day +30, the minutes will be drafted, approved by the PRIME and USAID and posted on the MATRIC website. This cycle will be repeated biannually.

SAG Composition

The SAG will be composed of nine (9) voting members, with a minimum of two (2) members with relevant expertise from SSA. A quorum will be defined as a minimum of five (5) committee members (with one (1) SSA representative). All efforts will be made to staff the SAG with a range of member expertise that can support and inform on all products and their potential to be successful. Efforts will be made to assure gender, race and geographical balance of the committee. Because of the need to ensure timely evaluations by MATRIX of CP and Technology Accelerator Domain 1 and 2 projects MATRIX leadership may request on a case-by-case basis a waiver from USAID to allow a quorum of 5 without a SSA representative.

The SAG expertise profile may consist of the following expertise.

1. Pre-clinical HIV prevention product development. This may include expertise in animal pharmacokinetic/safety/efficacy models required for assessing anti-HIV and/or contraceptive activity.
2. Regulatory. Required expertise should include experience in developing and evaluating pre-Investigational New Drug (IND), Investigational Device Evaluations (IDE) and development of regulatory submissions. Individuals from FDA and SSA regulatory bodies may be used.
3. IND-enabling safety and toxicology. Expertise in the conduct and interpretation of pre-clinical animal model safety, toxicology, and pharmacology studies, including familiarity with Good Laboratory Practices (GLP).
4. Chemistry, Manufacturing and Control (CMC). Expertise in a variety of formulations and analytical techniques, including familiarity with Good Manufacturing Practices (GMP).
5. Clinical trial operations and support. Expertise in the conduct of First in Human (FIH), Phase I, and Phase II clinical trial design and implementation of clinical studies in the USA and SSA.
6. Socio-behavioral sciences. SBR expertise in end-user product perception, acceptability of products/protypes, preferred characteristics of prototypes/products, and SBR outcomes for products in stand-alone research and/or in early phase clinical trials.
7. Marketing and Business case development. Expertise in health product marketing and cost considerations particularly in SSA. This may also include specific expertise in Human Centered Design (HCD).

Selected SAG members may have experience and expertise in one of more of the identified expertise.

SAG Member Nomination

Each new SAG member (serving for the first time) may be nominated by the PRIME, MATRIX Steering Committee (SC) or USAID. The PRIME will develop a nomination slate minimally consisting of one main candidate and if available a back-up for that candidate. The 2 candidates do not have to have identical expertise profiles. The proposed nomination slate will be communicated to USAID for their comments and concurrence. USAID will respond with either approval or disapproval of proposed members within five (5) business days. For disapproved candidates USAID will provide a written justification (email) for disapproval. The PRIME has five (5) business days to contest the disapproval(s). If disapproval stands the PRIME will then work to identify a replacement nominee. Upon USAID concurrence with the nomination slate the potential nominees will be contacted by MATRIX leadership or its designees to determine if the candidate is interested in participating. If the nominee agrees to serve an information packet will be sent to the nominee. The information packet may contain a summary of MATRIX products and partners, redacted MATRIX application, information on renumeration and engagement, and any additional information that maybe relevant.

SAG committee membership is envisioned to be dynamic and nimble, adjusting through management of expertise mirroring the development of the MATRIX products as progress is made and/or problems are encountered. Therefore, SAG members will only be engaged for a single meeting (except for the first year where members will be engaged for both meetings). Individual SAG members may participate in serial meetings, but there will be no anticipation of long-term SAG membership by its members, the PRIME or USAID.

SAG members must be able to provide unbiased assessments of individual CP and Technology Accelerator Domain 1 and 2 projects to support the stage-gating process. All SAG Candidates will undergo an assessment of real and potential Conflict of Interest (CoI) (see below). Every effort will be made to ensure SAG members are free of conflicts of interest (CoI) and follow MATRIX's CoI policies (see MATRIX MOP).

Special Case SAG Membership
USAID may require that a specific individual(s) be included in the SAG. These members will undergo and be subject to the same nomination process above. USAID will communicate their nomination to the PRIME and provide a picture, contacts, short biosketch and brief justification for inclusion in the committee. The PRIME will follow the contact and vetting schema above and determine the willingness of the nominee to participate. If the nominee is willing to participate MATRIX administrative personnel will proceed with onboarding for that specific meeting. If the PRIME or SC identifies a potential conflict or has a significant issue with the USAID nomination the MATRIX PRIME will submit in writing a rebuttal to the nomination within five (5) working days of receiving the nomination.

Inactive and Retired SAG Members
Given the proposed dynamic nature of the MATRIX research agenda and the desire to have a nimble, neutral, cross-cutting, multidisciplinary committee that has the appropriate expertise for each biannual evaluation, the PRIME may retain a list of approved but inactive SAG members.

Inactive SAG members will be individuals who have been approved by the nomination process and remain free of CoI.

Members may also be SAG retired. SAG members identified for retirement may no longer have relevant expertise to MATRIX projects. MATRIX will retire SAG members following consultation with USAID. A SAG member may also be retired due to unmitigable CoI and/or conduct or actions that are deemed inappropriate for a SAG member. Conduct/actions may include failure to attend meetings and lack of participation in meeting discussions.

Conflict of Interest (CoI)

The complexity of the MATRIX award and the interconnectedness of the HIV and prevention field may result in real and/ or perceived CoI with specific research project(s) and/or individual researchers involved in MATRIX. The SAG will follow the CoI policies laid out in the MATRIX MOP. MATRIX will work to manage both real and perceived CoI. SAG specific CoI policies follow.

SAG members must be free of competing CoI, i.e., significant involvement with a MATRIX research project and/or be employed by a pharmaceutical company supporting MATRIX developers. This prohibition applies to for-profit and not-for-profit individuals/companies supplying in-kind research material(s) such as drug product(s), drug substance (s), active pharmaceutical ingredients (API), and/or delivery devices/ device components for use by MATRIX researchers. Prior to installation on the SAG, committee nominees will sign a CoI and identify any potential real or perceived CoI. At the beginning and end of each SAG meeting a CoI declaration will be signed to ensure that any emergent conflicts among SAG members are captured and addressed.

It is acknowledged that there may be cases where a SAG committee members CoI cannot be avoided, and the expertise of the conflicted individual(s) is required to adequately advise the stage-gating process. In this case the conflicted individual(s) will act as an informational resource to the SAG. The conflicted SAG member(s) will be excused from voting on the product(s) for which they have a conflict. If the PRIME judges that the conflict will remain an issue in future SAG meetings the member maybe retired from active participation on the committee. The PRIME will inform USAID of this decision. A SAG member with CoI may also be retained as a consultant (active or ad hoc) to the SAG.

SAG Chair Responsibilities

The SAG Chair and alternate will be appointed by the PRIME. USAID will provide concurrence for the nomination. The SAG Chair and alternate unlike the SAG members, will be a member of the MATRIX team, and will not be directly involved in MATRIX supported research or activities. The SAG Chair and alternate will be non-voting members of the committee. In the case that the SAG Chair is not available the alternate chair will conduct the meeting. The SAG Chair and

alternate chair will be appointed for the duration of the award, unless otherwise determined (see below, Removal).

The SAG Chair will be responsible for coordination of the meeting and supporting activities (see below and Appendix 1 and 2). The chair will be assisted by the appropriate MATRIX administrative personnel. The SAG Chair's primary responsibility will be to manage the flow of the biannual SAG meeting to assure the meeting adequately evaluates the CP and Technology Accelerator Domain 1 and 2 projects under review. The SAG Chair is also responsible for assuring a clear outcome of SAG deliberations. To accomplish this the SAG Chair will be involved in pre-, during, and post-meeting activities (described below).

The SAG Chair will act as a liaison between the PRIME, SC, USAID, MATRIX PDL, and be responsible for assuring the SAG meeting achieves its objectives, adheres to charter policies, and accomplishes its agenda. Prior to each biannual meeting the SAG Chair will review the Milestone and Benchmark Reports (MBR), Mitigation Plans and New Project Requests (submitted one month prior to the meeting) and clarify with the PDL any issues that might have been identified. One (1) week before the meeting the chair will meet with the PDL to determine if there are any critical updates to the submitted report/plan. If there are updates the PDL (with support of the SAG Chair) will develop a brief (maximum one (1) page) addendum to the MBR. At this time SAG Chair and PDL will identify any specific questions the PDL wishes to pose to the SAG during the open session and prepare these for discussion during the open and/or closed sessions. During the meeting the SAG Chair will facilitate the discussion in the open session and when appropriate bring the open session to a close and initiate the closed meeting. In the closed session the SAG Chair will lead the SAG and facilitate voting on one of the defined SAG outcomes (see below). The chair will also assist the SAG in formulating any additional comments from the SAG to the PDLs. Post-meeting, the SAG Chair will provide, following approval of the PRIME and USAID, the final recommendation of the SAG and any comments to the PDLs. The SAG Chair will review the draft minutes of the meeting and assure they are posted to the internal MATRIX website within 1 month of the meeting.

SAG Final Opinion, Recommendations and Comments Reporting

The SAG Chair and assigned MATRIX administrative personnel will capture the final opinion and any additional comments and/or recommendations made by the SAG for each project during the closed sessions. The results will be collated for each project and assembled into a tabular form for distribution to the PRIME and USAID. PDLs will only receive the tabular form with any answered questions or additional recommendation for the specific projects they represent. The complete tabulated final opinion, recommendations and comments will be placed in a password protected section of the MATRIX website, available only to the PRIME, SAG Chair, USAID and individuals identified by the PRIME who need access to the document for administrative purposes.

SAG Chair or Alternate Removal

The SAG Chair or alternate may be removed as chair in the case of malfeasance, and/or development of a CoI with MATRIX product developer(s). Removal may be initiated by either the PRIME or USAID. Removal initiated by the PRIME requires concurrence by USAID.

Responsibilities of the PRIME

The PRIME will provide administrative support for all SAG operations including collating progress reports and communicating them to the SAG members, supporting meeting conduct (virtually or in person) and developing official minutes for the SAG open meeting sessions.
The PRIME will be responsible for communicating all SAG nominations and SAG personnel actions to USAID. The PRIME will identify a SAG Chair and alternate and present them to USAID for concurrence.

The PRIME will be responsible for liaising with USAID to obtain concurrence with SAG recommendations and approval for release of the recommendations to the PDLs

USAID Responsibilities

USAID personnel will be responsible for appointing and providing USAID employees to monitor the SAG meetings, and for providing approvals of SAG recommendations in a timely manner. USAID will provide approvals for SAG member nomination and provide appropriate input for disapproved nomination slate members. USAID personnel will work with the SAG Chair to develop any specific questions they wished posed to the SAG during the open and/or closed sessions. If questions arise during the SAG meeting USAID will pose them through the SAG chair to avoid interrupting the meeting.

SC Member Responsibilities.

The SC members of MATRIX are the leaders of each product development effort in the CP and oversee the activities of the Technology Accelerator Domain 1 and 2. The PRIME will engage SC members as needed to provide potential SAG nominees and other support as required by the PRIME. The SC member may also be the PDL designated to represent the project (s) to the open session of the SAG meeting. If the SC member is not the representing PDL, the SC member is responsible for appointing and preparing the PDL for the SAG meeting.

SC members will follow MATRIX MOP CoI policies and the specific CoI policies that apply to SAG operations. When conflicts are identified, SC members may be excused completely from discussion of CoI-involved issues or may be allowed to participate in a limited manner as an informational resource to the MATRIX PRIME, remainder SC and USAID.

MATRIX Product Development Leader (PDL) Responsibilities

A MATRIX PDL is anyone responsible for overseeing the conduct of research or MATRIX product development activities. The PDL maybe a member of the SC or an individual guiding or leading a project/subproject under a SC member. The PDL will liaise with the SAG Chair, and PRIME to facilitate the stage-gating process.

The individual PDL for both the CP and Technology Accelerator (Domains 1 and 2) are responsible for providing the MBR report cataloguing the progress made during the reporting period on the specific programs funded milestone(s), benchmark(s) and Go/No-Go criteria governing or relevant to enabling the stage-gating process. PDLs are also responsible for identifying the need for mitigations and developing a Mitigation Report for any Class 2 or 3 mitigation event (see below). PDLs are also the primary point of contact (POC) for the SAG Chair/alternate, in preparation for or following biannual SAG meetings.

One (1) week prior to SAG meetings the PDL and the SAG Chair will determine if there are any specific questions the PDL wants posed to the SAG or if there are any updates to the MBR that could impact SAG recommendations. These could include solution of a Class 1 mitigation finding and/or updating information on a milestone, benchmark, or Go/No-Go that could influence the SAG recommendation. If there are updates or questions the PDL will develop a brief (1 page) addendum to the MBR to be submitted to the PRIME, SAG Chair and USAID.

The PDL or a representative must attend the open session of the SAG meetings for their specific product(s). PDL will not be required to provide any formal presentations to the SAG and are present during the open session only to answer any questions the SAG may have for them. During special request evaluations (see below) the PDL maybe required to present a topic specific presentation to the SAG.

The PDL will not participate in the closed session of the SAG.

Responsibilities of the SAG Members

It is the responsibility of the SAG members to assure that their participation in the SAG meeting does not violate CoI policies of MATRIX and to be familiar with the MBR, Mitigation plans, New Project Requests and pre-meeting updates submitted by the PDLs. The SAG members are also responsible for keeping any written documents (e.g., MBR reports) and closed session discussion confidential. Each SAG member is encouraged to actively participate in the discussions. This participation is critical to achieving the end-to-end evaluation of the products and progress that the stage-gating process requires.

Requirements to Conduct a SAG Meeting

The SAG committee consists of a minimum of nine (9) members with a quorum defined as five (5) members either present in person, virtually or a combination of both modalities. A quorum requires the participation of at least one (1) SSA attendee. If delay of the meeting due to availability of a SSA member would adversely impact USAID/MATRIX work planning activities a USAID waiver specific to the proposed meeting for a five (5) member quorum without a SSA representative maybe requested by the PRIME. For each meeting the SAG members must commit to the equivalent of a full day of participation. A day's worth of participation maybe conducted as one contiguous day, or 2 half days as needed. A full day is defined as 9 hours, starting no later than 9:00 AM EST and ending no later the 6:00 PM EST.

SAG Meeting Overview

The biannual SAG meeting will be composed of 2 sessions: an open and closed session for each product development activity under review (CP, Domain 1, Domain 2). It is envisioned that each session (open or closed for each product) will take no more than 30 minutes and be facilitated by the SAG Chair or alternate. Appendix 2 contains a flow chart of the SAG meeting.

The official meeting will start with the SAG Chair calling the meeting to order.

The SAG Chair will welcome the SAG members and each member will introduce themselves. Any personnel present representing the PRIME, MATRIX administrative personnel, and USAID will identify themselves and their responsibilities/reason for attendance. PDL representatives will not be present, during this portion of the meeting. Open Session representatives of the PRIME, USAID and administrative personnel responsible for minutes and meeting conduct will be present as observers only and will not actively contribute to the meeting unless specific questions are addressed to them by the SAG, thru the SAG Chair.

The SAG Chair will read aloud the MATRIX CoI policy and then administrative MATRIX personnel, if the meeting is in person, will collect signed CoI forms. If the meeting is virtual or a SAG member is virtual MATRIX administrative personnel will facilitate obtaining a signed COI. If new CoI is identified by a member, it will be determined by the PRIME and chair if the SAG member should be excused from a specific product stage-gating discussion and/or participation be limited to a non-voting presence. Concurrence will be requested from attending USAID personnel.

The SAG Chair will ask for approval of the minutes of the last meeting by a nomination, second, and show of hands. If the SAG members pose an objection or request modifications, after resolution of the issue(s) the SAG Chair will ask for a motion to approve and second. The minutes will stand as approved.

The meeting will proceed to the order of business. Prior to the start of the first open session the SAG Chair will review the agenda of projects to be discussed.

The SAG Chair at this time will identify any projects that do not require extensive discussion and maybe triaged (see below). If there are no PDL questions or other issues the SAG Chair may recommend that the project be assigned a “Continue as Planned” outcome with a majority vote of the SAG. If continued as planned vote is not unanimous the minority opinion will be captured and placed in the minutes and an open and/or closed session be conducted, as required. For projects with specific enquiries to the SAG that are proposed and approved for triage an open session will be used to provide the PDL feedback on their questions.

The first open session will be initiated. The PDL will be invited into the meeting and introduced. The open session will consist of a discussion of the PDL MBR and/or Mitigation Plan or New Project Request. Discussion will be facilitated by the SAG Chair. At the beginning of the open session the SAG Chair will summarize the information in the MBR (and Mitigation plan, if included), any additional last-minute information and questions. During the open session the SAG members will discuss the MBR/Mitigation Plan/New Project Request and may ask clarifying questions of the PDL. The SAG, thru the SAG Chair, may ask procedural questions of USAID and/or the PRIME. No specific recommendations will be made during the open session (see below). At the end of the open session the SAG Chair will summarize the discussion and the PDL will be excused, and the session closed. Minutes will be taken during the open session if in person or recorded if virtual.

The closed session will be started by the Chair. During the closed session the SAG may openly discuss the reports and provide their final evaluation, making 1 of 6 possible evaluative recommendations of the project under discussion (Table 1). After the SAG meeting is closed USAID will provide concurrence or disapproval for each SAG recommendation. Specific minutes or recordings of the closed session will not be taken and only the final evaluations and any additional specific recommendation(s) of the SAG will be reported.

Table 1 Summary of SAG Recommendations

Recommendation	Comment	Applicable to:		
		CP	Domain 1	Domain 2
Continue as Planned	All activities	X	X	X
Discontinue Activity	• CP all or Selected Parts • Off-Ramped Domain 2 • Domain 1	X	X	X
Off-Ramp Domain 2	All or Selected Parts of CP	X		
On-Ramp To CP	Return To CP			X
New Project	CP Domain 1	X	X*	
Disapprove New Project	CP	X		

* Review of new Domain 1 Technology Accelerator projects by the SAG is a complimentary review to familiarize the SAG with the new Domain 1 project,

SAG Recommendations
The SAG may make the following recommendations for each project reviewed.

1. Continue as planned for CP or Technology Accelerator projects (Domains 1 and 2). The SAG does not recommend any changes to the proposed development activities based on the MBR, but may provide recommendations for the PDL and team to consider.
2. Discontinue the Activity.

- Technology Accelerator Domain 1. This will be closing out the project activities.
- CP off-ramped projects in Domain 2. The activities will be stopped and close out activities performed.
- CP projects. The recommendations will include either a direction to stop and close out all activities or to continue specific activities within the project that the SAG deems of high value. USAID must concur with this recommendation.

3. Off-ramping from CP to Domain 2 of the Technology Accelerator. If a CP project has a significant mitigation finding (class 2 or 3), the SAG may recommend off-ramping to Domain 2 of the Technology Accelerator. If a Mitigation Plan was not attached to the MBR (see below) the PDL in collaboration with the PRIME will create a Mitigation Plan specific to the planned Domain 2 activities.
4. On-ramp/return to CP a previously off-ramped (Technology Accelerator Domain 2) CP project following resolution of the mitigated problems. This recommendation applies only to Off-ramped CP projects.
5. New Projects. Following the Technology Accelerator Domain 1 procedure for selection of new projects, the SAG will review the new project to increase familiarity of the SAG with the project for future meetings. (See New Projects section below and the new project request form Appendix 5). In this case the SAG will be asked to provide concurrence to the Domain 1 on-ramping. Following a positive recommendation, USAID with the PRIME will decide if the project will be added to the MATRIX Portfolio.
6. Disapprove on-boarding of new CP project. The new CP project will not be on-boarded by MATRIX, following USAID concurrence.

Disagreement of USAID with Final SAG Determination

USAID has the right to overturn all SAG final determinations as the funder of the MATRIX consortium. It is expected that these disagreements will reflect broader USAID operational issues beyond the drug development progress the CP or Technology Accelerator projects has made and may be independent of the achievement of milestones, benchmarks, and Go/ No-Go criteria. In these cases, USAID will provide a justification for overturning the SAG recommendation that will be placed in the record of the SAG meeting. The new recommendation will be placed in the final outcome section of the MBR, Mitigation Plan and New Project Request. It will be at the discretion of USAID to provide further information to the PDL on the decision and how to communicate the change to the SAG.

Project Triage at the Start of SAG Meetings

Because of the number of projects in the MATRIX portfolio and to facilitate a one-day meeting a triage process may be used at the start of the meeting. This triage process will only be for projects that indicate in the MBR that they are proceeding as planned. Projects with an active Mitigation Plan are not eligible for triage. Projects eligible for triage as determined by the PRIME and USAID will be introduced at the beginning of the meeting by the SAG Chair and if there are no SAG objections or concerns the project(s) will be assigned “Continue as Planned” and no copen/closed session conducted.

If the SAG expresses concern regarding the triage, the SAG will be asked if they require the PDL for consultation in an open session or want to proceed into the closed session for discussions with the PRIME and USAID regarding their rationale for triage. The SAG will decide this by majority

voting. If the SAG requires PDL input, an open session will be started and the PDL will be invited into the meeting where the SAG may propose specific questions to the PDL. Once the SAG is satisfied the PDL will be excused, and the meeting proceed into a closed session. If the PDL is not needed the meeting will proceed directly to the closed session. In a closed triage discussion session, the SAG may directly question the PRIME and USAID regarding the decision to triage. For cases where there is disagreement within the SAG about tirage or the meeting proceeds to a closed triage session any minority opinion(s) will be captured in the open meeting minutes.

Futility Determinations

Futility is defined as a project that no longer demonstrates a reasonable chance of completion during the award, a major experimental failure/finding that raises significant concerns regarding the ability to meet long-term milestones, benchmarks, and/or Go/ No-Go criteria, or advances in HIV virology, and/or the prevention field render the proposed innovation no longer of significant value to USAID. A SAG majority is required to recommend futility.

There are 2 scenarios under which the SAG might recommend futility.

- The first is concurrence with a request by the PRIME and USAID to assign futility to a CP, Domain 1 or Domain 2 Technology Accelerator project. A determination of futility maybe requested based on MDR reports, PDL use of serial mitigations of any class within a project, failure of a Mitigation Plan and/or a USAID research or fiscal priority. Because the action is requested by MATRIX leadership and USAID, a simple majority will be used for approval. Any dissenting opinion(s) will be captured.
- The second is a recommendation made by the SAG during a closed session based on the contents of a MBR report and/or past performance (MBR content, serial mitigations, etc.). In this case, a majority of the SAG must recommend futility. The dissenting opinion will be captured.

In all cases, action upon a futility recommendation must be ratified by USAID before any is taken to end the project.

Mitigation

Because research is under the influence of both inside (experimental design failure) and outside (availability of reagents, administrative approval delays, etc.) factors that can impact the accomplishment of R&D objectives for the overall or specific parts of an R&D plan, proactively addressing these issues by planning their resolution can reduce the impact of these events on achievement of milestones, benchmarks, Go/ No-Go criteria. Therefore, MATRIX has instituted the use of Mitigation Plans with SAG evaluation as a tool to proactively address and manage R&D delays. The template for the Mitigation Plan can be found in Appendix 4. A Mitigation Plan is defined as a PDL proposed, proactive plan designed to address unexpected experimental delays and minimize their impact on the overall R&D effort by proposing a specific set of experiments to address the mitigatable issue. A Mitigation Plan is developed by the PDL with or without input of the PRIME and USAID and evaluated by the SAG for the purposes of monitoring progress and making additional recommendations to the PDL, PRIME and USAID. The SAG may also recommend creating a Mitigation Plan based on the MBR report.

There are two types of mitigations.

- The first is a request by the PDL based on findings reported in the MBR. In this case, the Mitigation Plan will be attached to the MBR and evaluated by the SAG.
- The second case is when the SAG determines there is a need for mitigation, based on the contents of the MBR and open session responses of the PDL.

The SAG will be asked to provide input on Mitigation Plans for Class 2 and 3 mitigations (see below) when they are provided with the MBR. If a class 2 Mitigation Plan extends beyond 6 months (1 reporting interval) or a class 3 Mitigation Plan extends beyond 12 months, the SAG will be asked to consider if or when a recommendation of futility is appropriate. If the SAG provides a futility recommendation it will be passed to the PRIME and USAID for action. All futility recommendations will be done by majority voting. If the voting is not unanimous the minority opinion will be captured and communicated only to USAID by the PRIME.

In the second case, The SAB identifies concerns that they believe are either mis-labeled as a Class 1 Mitigation (see below) or based on the MBR identify a critical issue(s) that is not being addressed but must be mitigated prior to achieving the projects Gantt's milestones, benchmarks, Go/No-Go criteria and TPP specifications. In this case, the PRIME and USAID will instruct the PDL to create a Mitigation Plan. To reduce the delay between mitigation report, approval, and implementation USAID and the PRIME will evaluate and approve the plan outside of the SAG review process. The need for a Mitigation Plan will be communicated to the PDL immediately after the meeting and with the plan due in two (2) weeks to the PRIME, and USAID. The plan will be approved or disapproved in one (1) week. At the next SAG meeting the new Mitigation Plan will be attached to the MBR and reported to the SAG for consideration during the closed session.

New Projects

The HIV prevention field is dynamic in nature and requires a nimble approach to addressing and creating the optimal prevention strategies for AGYW, PBFW and FSW in SSA. Additionally, there can be specific barriers to implementation of a HIV prevention strategy, such as the need to monitor point-of-care drug concentrations, engineer health care professional friendlier device application and removal processes, etc. Thus, the potential for identifying and implementing new projects both for the CP and Domain 1 Technology Accelerator has been incorporated into MATRIX. A new project is defined as a scientific opportunity that has a defined scientific/experimental approach that if successful could add significantly to the USAID prevention portfolio or their efforts to implement the portfolio. These opportunities have often been identified as "game changers" if successful. The template for the New Project Request is in Appendix 5. Final approval to implementation new projects is under the control of USAID.

At the end of a SAG meeting in an open session the SAG will be asked to consider whether to recommend on-ramping of any new CP. SAG members will be asked to provide a majority opinion for either approval or disapproval for the on-ramping request. The SAG will identify the potential and specific advantages of addition of the proposed CP activity to MATRIX. The recommendation will be forwarded to USAID for final ratification or rejection. No closed session discussions will occur. For new Technology Accelerator Domain 1 projects the SAG review will be used to familiarize the SAG with the new Domain 1 project. Since the new Domain project will have undergone approval using the Domain 1 on-boarding process which includes USAID approval, the SAG will be asked to concur and provide any specific recommendations, if appropriate,

Meeting Format

The SAG meeting with a quorum of SAG members will be conducted in one of 3 formats.

1. Virtual,
2. In-person,
3. Hybrid: mixture of virtual and in-person attendance.

A quorum is defined as a minimum of five (5 SAG voting members, whether in person, virtual or hybrid. When scheduling meetings every effort will be made to assure participation of one (1) or more SSA SAG members. In special cases a waiver for the meeting to be conducted may be obtained from USAID to complete a quorum if availability of the SSA SAG member negatively impacts the ability to conduct a SAG or impacts negatively on USAID workplan development.

For meetings with an in-person component written minutes will be taken, If the meeting is fully virtual the meeting will be recorded, and a written transcript developed. During virtual or hybrid meetings, virtual members must be present and vote for a minimum of 2/3 of the projects on the agenda for which they have no CoI.

Voting

Voting will occur during the closed session and will be conducted by the chair asking each member for their vote.

Based on the open meeting, the chair will summarize the discussion and identify potentially relevant voting outcomes (discontinue/stop, continue as planned, create a Mitigation Plan, etc.) for the report/project under discussion. New Project Requests will not have a closed session (see above). The SAG Chair will then call upon the SAG members to vote. If the vote is not unanimous, the chair will facilitate a discussion to determine if a unanimous opinion can be reached. If an unanimous opinion cannot be reached; the majority opinion will be provided to the PDL and published on the internal MATRIX team web page (see Communication below).

If a consensus cannot be reached the SAG Chair will ask for the minority to provide a brief written statement of the issue driving their opinion. The minority opinion will be provided to the PRIME and USAID and they will decide if the minority opinion is provided along with the majority opinion to the PDL and/or placed on the internal MATRIX team web page.

If the SAG or any of its members want to make a specific recommendation(s) to the PDL during the closed session they may do so. If additional recommendations are made, the chair will ask for a vote in support of the recommendation. All recommendation communicated to the PDL must be approved by a majority of the SAG members present. If a majority in favor of the recommendation cannot be obtained an official recommendation will not be sent to the PDL.

Mitigation: Plans and Classification

It is recognized that unexpected problems may arise that have minor to catastrophic impacts on product development activities. In order to facilitate SAG review, the following mitigation classifications (below) will be used to describe these problems. The classification system is in place solely to facilitate SAG, PRIME and USAID actions, and thus uses a broad classification system for its assignments. The Mitigation Plan and the classification system have been developed to assist CP and Technology Accelerator (Domain 1 and 2) PDL in resolving, in a timely manner, technical issues that impact milestone, benchmark, Go/No-Go criteria and TPP specification achievement. Mitigation Plans will be used for both CP and Technology Accelerator (Domain 1 and 2) projects. If the mitigation is reported in the MBR its classifications will be made by the PRIME and PDL prior the SAG meeting, USAID may be consulted on the classification. If a recommendation is made by the SAG, the Prime and USAID will create the classification based on communication with the PDL and approve the PDLs Mitigation Plan.

Mitigation Plans will not be used for Technology Accelerator Domain 1 projects, since they are predicated on providing a proof-of-concept for a specific hypothesis and outcome is measured by either success or failure in achieving that outcome in a timely manner.

Mitigation Classes

Class 1: Minor or transitory delays in research. The resolution of class 1 mitigation issues is in general out of the hands of the PDL. The resolution of the mitigation issue is reasonably expected to take no more than 6 months or 1 SAG reporting interval. Examples of this type of mitigation are timing of animal studies by CROs, delays in IACUC or IRB approvals, natural disaster delays, PDL institutional administrative delays, regulatory delays, etc. In this case, the PDL will place an explanation of the delay in the MBR report and provide a projected best- and worse-case resolution scenario, timeline, as well as alternatives, if any (e.g., alternative source or CRO) to resolve the issue if it cannot be resolved in the SAG reporting interval. Due to the nature of class 1 mitigations, there is no plan for upgrading the mitigation classification to a 2 or 3, however, futility maybe called if the delays become extensive >6-12 months and/or negatively impact the achievement of project milestone(s). An example of such a delay is extensive delay in SSA regulatory approvals for starting a single site in a multi-site clinical trial that jeopardizes progress, where the sites in question participation maybe compensated by other sites where regulatory approval has been obtained. In this case a futility designation (as described above) may be requested by the PDL for the class 1 mitigation or independently made by the PRIME, and USAID. The SAG will be informed that activity has been removed from consideration at the next meeting.

Class 2: Moderate Delays in Research. These are cases where a resolution of the issues encountered are possible within a limited time frame which will not significantly impact overarching milestones (i.e., clinical testing in 4 years) benchmarks, and Go/ No-Go criteria but require a focused research effort to keep the R&D process on track. Class 2 mitigations should be resolved as quickly as possible. It is expected that resolution of a class 2 mitigation could take more than 6 months but are likely to be resolved in less than 12 months. Examples are minor modifications of formulations to meet stability requirements, need for a minor modification of a synthetic or manufacturing process, minor adjustments to formulations or delivery devices to meet desired/pre-defined rheological properties, etc. In the case where the class 2 mitigatable finding is discovered in the interval between SAG meetings, the PDL with the PRIME and USAID will agree mitigation is appropriate and they will work with the PDL to create a Mitigation Plan

(Appendix 4). The Mitigation Plan will be attached to the MBR and communicated to the SAG at the next biannual meeting.

Because of the expected quick resolution of class 2 mitigations, it is not expected that these mitigations will initiate off-ramping to Technology Accelerator Domain 2. However, if mitigation efforts extend beyond 12 months, with the consent of the PRIME and USAID, the mitigation can be reclassified as a class 3 and the project moved to Domain 2 of the Technology Accelerator. Off-ramped projects of this type are subject to class 3 mitigation and serial mitigation rules (see below).

Class 3: A severe to catastrophic problem/delay in product development that could either completely halt development (fatal flaw in drug substance or product) or delay development for an extended period of time (>12 months) is identified. Examples are failure of a stability program that indicates major changes are needed in the formulation or API, a serious safety finding or adverse event in preclinical or clinical studies, respectively, failure of GMP manufacturing or meeting GMP quality requirements. Similar to class 2 mitigations a class 3 mitigation can be discovered between reporting intervals or at the SAG meeting, in both cases the procedure to initiate, approve and SAG review the plan will be used.

A critical part of any class 3 mitigation will be a determination if all or part of the parent CP project requiring mitigation needs to be off-ramped to Technology Accelerator Domain 2 and whether other activities within the CP should continue while the component is off ramped, with or without modification. The SAG will recommend off-ramping and whether other activities in the CP should be continued. USAID will determine if these recommendations are followed.

Class 3 Mitigation Plans will be submitted to the SAG for review at a regular scheduled meeting. Because it is expected that class 3 mitigations are of sufficient severity to trigger off ramping to Domain 2 and that success of off-ramped projects are directly tied to the potential success of the CP project it is expected that the majority of class 3 mitigations will automatically be off-ramped to Domain 2.

SAG review of ongoing projects with a Mitigation Plan (class 2 or 3) may result in the following recommendations by the SAG.

1) Mitigation efforts should continue as planned. The SAG will estimate the likelihood that resolution of the mitigation within the CP or off-ramped Domain 2 project will be completed in the projected time; however, if the problem is not resolved within a reasonable timeframe (see above class 3 definition) the SAG will be asked to consider recommending futility. Additionally, if the SAG believes the likelihood of resolution is low the SAG may recommend futility and stopping of activities. Policies for futility (above) will be followed and USAID approval obtained.

2) Development is terminated with or without continuation of other specific CP activities. If other activities in the CP are identified as providing significant advantage to MATRIX and USAID, then the SAG may recommend they be continued. Domain 2 off-ramped projects with this recommendation, since they are focused on a specific

mitigation effort, will not be considered for partial restoration or preservation of research activities (will not be automatically moved to Technology Accelerator Domain 1 or retained in Domain 2 beyond the futility/stop recommendation). USAID will approve the final determination. If there are other CP activities to be continued, they will continue to be reviewed by the SAG and held to their milestones, benchmarks, and Go/ No-Go criteria. An example is although product development cannot continue without a major reengineering of the drug product, ongoing behavioral social research, users' preferences, business case determinations, and/or marketing assessments could provide substantiative information of benefit to MATRIX and the USAID research agenda.

3) Return to CP of a Domain 2 activity. The PDL with consent of the PRIME and USAID, may request that the off-amped project be returned to the CP following resolution of the mitigation issues. The SAG will review the request and with appropriate evidence in the MBR recommend return of the off-ramped activity to the CP. The PRIME and USAID will review the recommendation and approve or disapprove re-ramping and continuation of the restored CP project.

SAG Identified Mitigations

The SAG may identify a mitigatable issue during a scheduled meeting and recommend it be addressed with a class 2 or 3 mitigation. The SAG will describe the proposed mitigation, classify the mitigation, identify what a potential resolution looks like and recommend that the PDL creates a formal Mitigation Plan based on their recommendations. The PRIME and USAID will confer and if appropriate direct the PDL to create and implement a Mitigation Plan. The Mitigation Plan will then be evaluated along with its associated MBR at the next SAB meeting.

Serial Mitigations

Serial mitigations are defined as multiple mitigations (class 2 or 3) for one project (CP) or requesting additional mitigations (CP or Domain 2 off-ramp) while a current mitigation is ongoing. Mitigations are meant to be used to provide a safe space where a defined problem can be resolved, while minimizing its impact on milestones, benchmarks and Go/ No-Go criteria being used to measure overall CP progress. Multiple mitigations may be considered as evidence of a problematic R&D effort, drug and/or delivery system. PDLs that request multiple class 2 and 3 or concurrent mitigations may undergo a special evaluation (see below) at the request of USAID and/or the PRIME.

Special Considerations for Domain 1 Technology Accelerator Mitigations

Domain 1 Technology Accelerator projects are special proof-of-concept projects projected to have a high value or be game changes for USAID and MATRIX. As such they are working toward specific goals and milestones designed to provide a proof-of-concept/hypothesis for the supported R&D project. Examples may be demonstrating that a specific instrument has the sensitivity and specificity to allow drug detection at point-of-care sites or a novel polymer system provides superior rheological/biological properties versus an established system. Although Domain 1 projects are subject to SAG review and MBR reporting, it is not expected that they will be subject to class 2 and 3 mitigations. MBR reporting and SAG evaluations for Domain 1 projects will be focused on achievement of the milestone(s), benchmark(s), Go/No-Go criteria that demonstrate

the value of the new technology/information/mentorship success, etc. Therefore, SAG evaluations will have one of three outcomes:

- Domain 1 objectives have been met and project stops,
- Continue project as planned,
- Discontinue project given information that objectives are unobtainable or cannot meet projected specifications of the technology being developed (sensitivity, specificity), safety, efficacy and/or pharmacokinetic parameters.

Special Case: Domain I On-Ramping to CP
There is the potential for Technology Accelerator Domain 1 projects that are highly successful and have such a significant impact to warrant on-ramping to the CP. Consideration for this type of on-ramping will be initiated by USAID in collaboration with the PRIME. Central to this on-ramping process will be the provision of budgets, Gantt chart with milestones, benchmarks, and Go/No-Go criteria, timeline, project descriptor, and TPP that supports the projects as having significant value to USAID and MATRIX. These projects once identified for on-ramping will be introduced to the SAG and undergo routine SAG evaluation.

Confidentiality of the SAG Meeting

Because the SAG meeting will generate outcomes that maybe critical of a product development (CP or Technology Accelerator Domain 2) or Technology Accelerator (Domain1) effort and result in negative outcomes for the developer (i.e., reduction of or loss of funding), it is critical that the closed deliberations of the SAG committee remain confidential. SAG members will be reminded at the close of the meeting that all closed session discussions are confidential and that only the final recommendation and a minority opinion, (if applicable) will be communicated to the PDLs. The SAG members will also be instructed that if they are contacted by a PDL for specifics about the closed meeting that they are not to divulge any information and contact either the SAG Chair and/or PRIME.

Deliverables to the SAG Milestone Benchmark Report (MBR), Mitigation Plan and New Project Reports

Milestone Benchmark Report (MBR)
One (1) month prior to the scheduled SAG meeting the PDLs will submit a MBR for each project identified for stage-gating by the PRIME. The template for the MBR can be found in Appendix 3.

The MBR will consist of:

- A general project description (200 words or less) that describes the product and drug delivery system and current status. This portion of the report should remain relatively constant with minor changes, except in the case of a major status change, e. g. off-ramping.
- A tabular summary of progress for milestones, benchmarks, and Go/No-Go criteria. This table will provide a concise summary of the progress on milestones, benchmarks, and

Go/No-Go criterion achieved or partially achieved during the reporting interval. It will also identify if a mitigation is required and provide a preliminary mitigation class assignment. Each milestone, benchmark, and Go/No-Go criteria will have a declarative statement of achievement with or without a statement of the problem encountered in meeting it.

- The MBR report will have a one (1) page progress narrative of the achievement(s) and description(s) of the problem(s) encountered. If a class 1 mitigation event is encountered, it will be described and its proposed resolution summarized. No further information will be required at this time. If a class 2 or 3 mitigation is identified a Mitigation Plan will be developed and attached to the MBR.
- Developers may opt to include an appendix (Appendix 2 of the MBR) with specific supporting data, if desired. If an appendix is used the PDL must actively cross-link clickable key index words within the MBR to the corresponding Appendix 2 data. The appendix should be no more than five (5) pages. The SAG will be under no obligation to read the appendix.
- Appendix 3 of the report will contain a tabular format budget summary, noting any budget revisions.
- If a class 2 or 3 mitigation is required, the PDL will complete and attach a Mitigation Plan to the MBR (Template in Appendix 4).
- The MBR contains additional appendices required by USAID. Appendix 5-7 are the project descriptor, Gantt chart and TPP submitted with the original MATRIX application. They will be updated as the CP project progresses, with changes captured in red. Appendix 8 is the USAID Microbicides R&D Assessment, which will be updated, if required, at each MBR report.

Mitigation Plan

If class 2 or 3 mitigation issue(s) is/are identified by the PRIME, USAID or PDL a Mitigation Plan (Appendix 4: template attached) is required. This report should be included with the MBR if the mitigation is identified prior to the SAG meeting or generated after the SAG meeting if mitigation is identified by the SAG or USAID. In general, the Mitigation Plan contains a brief description of the issue to be mitigated, an assessment of how it impacts the existing development plan and a description of the activities to be performed to mitigate the issue. Appropriate milestones with specific benchmarks and Go/No-Go criteria are identified. Objective, observable milestones benchmarks, Go/ No-Go criteria, and timelines are created to support that the mitigation has been successful. Any budget implications are also included. If it the mitigation is for a CP project, a rational for continuation or pausing other project activities while the mitigation is in process is included. The PDL can request that his/her project be directly off-ramped into the Technology Accelerator Domain 2 for a class 3 mitigation effort. The SAG will be asked for their concurrence if the PDL asks for off-ramping. USAID will make the final decision for whether the project can be off-ramped and appropriateness of the proposed milestones, benchmarks, and Go/ No-Go criteria.

New Project Requests.

The SAG will review New Project Requests for CP and Technology Accelerator Domain 1 inclusion by investigators inside and outside of MATRIX. New projects may be designed to assist/mentor SSA investigators in developing their own HIV prevention long-acting or MPT

strategies, gain expertise in HIV prevention and drug development methodologies and/or establish regional and/or local HIV drug development and prevention expertise. New products may also be proposed for CP projects for the development of new long-acting HIV prevention strategies and/or MPTs. New Domain 1 projects are proposed to support innovative innovative/proof of concept development of a new drug, delivery system or technological innovation that supports the development of HIV prevention strategies and USAIDs mission. The request will be made using the New Project Request template (Appendix 5).

The SAG will review 2 types of requests for new research projects.

1. New CP Projects: The SAG will perform a full evaluation for new CP project requests and make recommendations to PRIME and USAID to either on board or not to onboard the new CP project. Following the meeting USAID will determine if the project will be onboarded. These projects will require the establishment of a project descriptor, TPP, Gantt chart, and USAID Microbicides R&D Assessment, in addition to establishing milestones, benchmarks, and Go/No-Go criteria for the research and provide a 1-year detailed budget.

2. New Domain 1 Technology Accelerator Projects: The SAG will perform a courtesy evaluation of new Domain 1 projects identified for onboarding. These projects will have undergone preselection by the Domain 1 on-boarding process and have been approved for participation in the Technology Accelerator Domain 1 prior to the SAG meeting by USAID. The SAG evaluation will be to familiarize the committee with the new project for future SAG meetings and to establish formal timelines, milestones, benchmarks, and Go/ No-Go criteria for future SAG evaluations. A product summary and TPP are only needed if the project is developing a long-acting anti-HIV antiviral or MPT.

Special Case: New Projects Derived from Terminated Technology Accelerator Domain 2 or CP Projects.
In rare, select cases terminated project elements may be eligible for new project consideration. The new project element for consideration must contain highly innovative game changing research which the PRIME and USAID identify as high-value that may provide proof-of-concept or preliminary feasibility data for future development activities (inside or outside MATRIX). The PRIME with USAID concurrence will decide the scope of the new project and invite the PDL of the terminated activity to make a topic focused New Project Request submission. These projects will be given a full review by the SAG and either approved or disapproved for onboarding. The new project request will require identifying milestones, benchmarks, and Go/No-Go criterion to measure research progress and achievement of the new project objectives. An impact statement will also be required identifying the specific value of the "rescued" project to USAID.

Special evaluations
At the request of the PRIME or USAID the SAG may be asked to evaluate a project (CP or Technology Accelerator Domain 1 or 2) even if it is currently on schedule and meeting milestones, benchmarks, and Go/No-Go criteria. Special evaluations are triggered by the emergence of evidence and/or new data from within MATRIX or the HIV prevention field that could make an existing MATRIX project activity no longer relevant to MATRIX and/or USAID priorities. Examples of the types of data that could trigger a special evaluation are BC evaluations

demonstrating significant impediments to post approval marketing or use, SBR data that reduces the confidence that target populations will use the prevention innovation, safety/implementation issues from other products developed outside MATRIX that suggest lack of efficacy, effectiveness or harm to users by the MATRIX product and/or opinions/interactions with regulatory bodies that suggest that current data portfolios or portfolios under development by PDLs will not support regulatory approvals (pre-IND, IND, New Device Exemption (NDE), New Drug Application (NDA), etc.). The goal of the special evaluation will be to assess the viability of the overall activity with a final determination by the SAG of continue as planned, modify plans or halt activity. For these evaluations ad hoc SAG members with expertise in marketing, cost analysis, business case development and post-licensure manufacturing, distribution and marketing may be added to the SAG. For these meetings, the PDL maybe requested to provide a specific update at the meeting. In this case the PDL may be requested to present relevant information in PowerPoint format with a 15 min time limit.

Communication and Documentation

SAG communication and documentation practices will follow all MATRIX MOP procedures for internal/external communication, documentation, and computer security. Every effort will be made to maintain confidentiality of the records generated during support and conduct of SAG meetings. Below are communication, documentation and security practices specific for SAG operations.

The open and closed segments of the SAG meeting will be documented as follows. The open session will be documented using either administrative minutes (in-person sessions) or by unedited recordings and their transcription (virtual). For hybrid sessions administrative minutes will be captured and a transcribed recording provided of virtual portions of the meeting. Minority opinions for specific activities (identified above) will be captured as indicted. Minutes during drafting and approval will be placed in a password protected section of the MATRIX4prevention.org website. PRIME, PRIME designees, SAG Chair and USAID will have password protected access to these documents.

PRIME designees may include MATRIX administrative personnel responsible for minute taking, drafting, and posting and the SAG Chair and alternate. PRIME designees will only be individuals without or managed CoI with CP, and Technology Accelerator Domain 1 and 2 Projects.

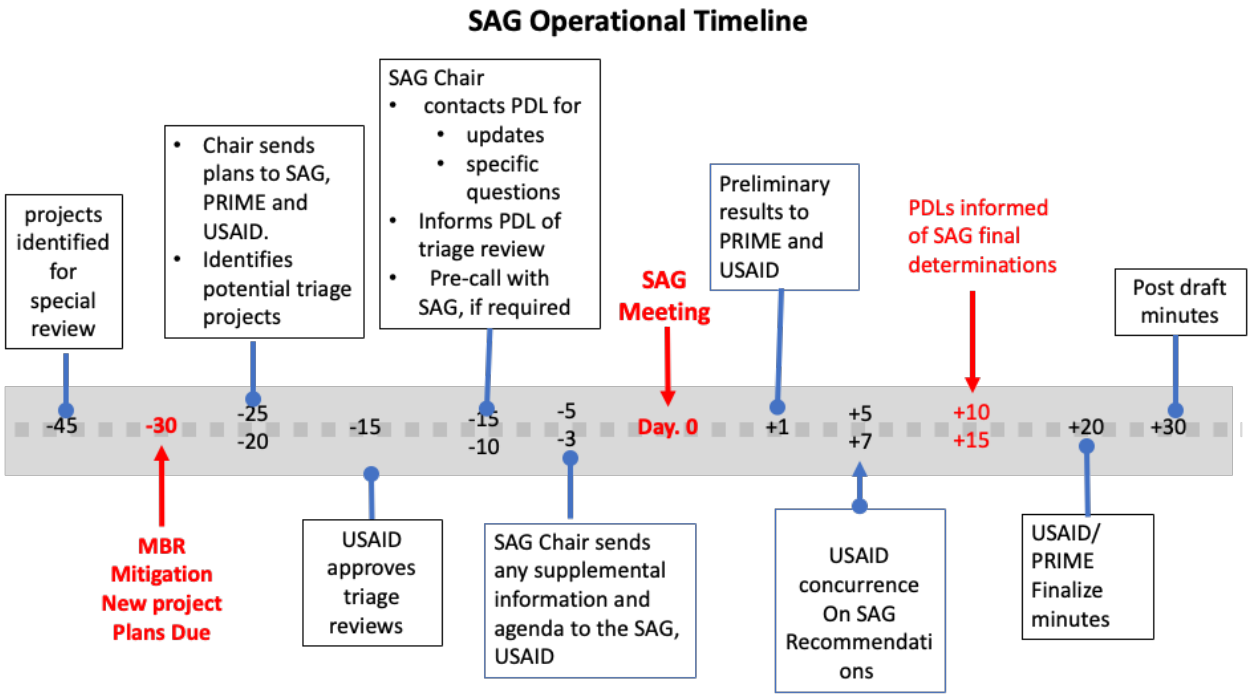
Communication and documentation of SAG outcomes to PRIME, SC and USAID will be a 2-stage process. Stage 1 will be approval by the PRIME and USAID of the SAG outcomes. Following the meeting the SAG Chair will submit the results of the closed session to the PRIME and USAID for concurrence with the SAG. Once concurrence is received the outcomes will be posted in a secured section (access by PRIME, PRIME designees, SAG Chair, and USAID) on the MATRIX4prevention.org website. If USAID does not concur with the SAG an explanation for the lack of concurrence will be documented by USAID and placed with the SAG recommendation on the secure team website. Stage 2 will be approval of the SAG meeting open session minutes. Post meeting the SAG Chair will work with the MATRIX administrative group to assemble a draft minute's document. The draft minutes will be submitted to the PRIME and USAID for

concurrence. The minutes will then be submitted for approval by the SAG at the next meeting using the process described above, the minutes after SAG approval will be posted in a secure section of the MATRIX4prevention.org website. Virtual recordings will be transcribed and follow the same posting and approval process. The actual recording will be destroyed.

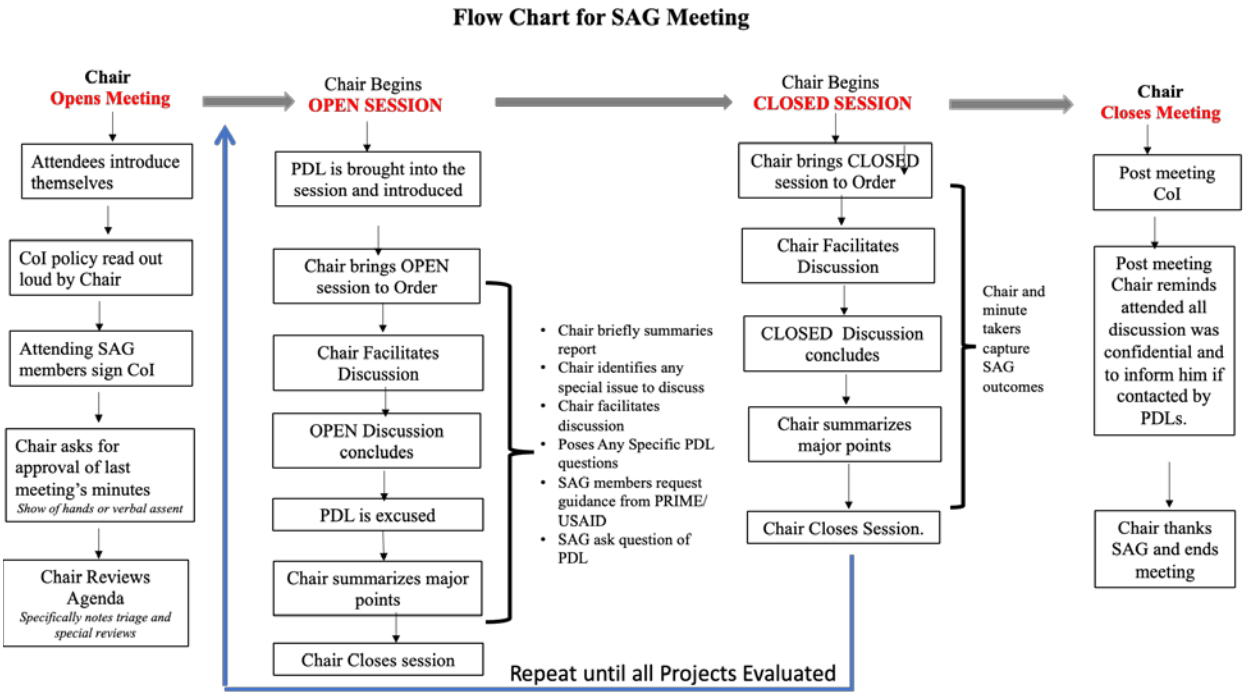
Final SAG recommendations will be placed in a non-public password protected portion of the MATRIX4prevention.org website. PDL will have password protected access to the final recommendations.

MBR, Mitigation Plans and New Project Requests will be placed in a non-public password protected subsite in the MATRIX4prevention.org website. Only the PRIME, PRIME designees, PDL, PDL designees, SAG committee members and USAID will have access to these documents. PRIME designees will include the SAG Chair, alternate chair, and administrative personnel responsible for report curation. The summarized results of SAG deliberations (final determination and specific recommendations) will be summarized and posted without access restriction to MATRIX team members on the internal MATRIX4prevention.org website. Summaries of MATRIX activities may be placed on the external public website, that may include outcomes of SAG evaluations. These postings will be redacted for confidential, sensitive, and intellectual property information and the content approved by the PRIME, SAG Chair and PDL.

Appendix 1: SAG Operation Timeline



Appendix 2: Flow Chart for SAG Meeting



Appendix 3: MBR Report Template

MDR reports must be in Microsoft Word with 12-point Times new Roman Font. All margins should be set a no less than 1 in. and must include the document headers and footers. Figures should be legible with no more than 150% magnification in MS Word. Reports that do not conform with formatting requirements and/or page and word limits will be returned as non-compliant

Date: Date of SAG meeting
Group/Organization:
Product: *Drug/delivery system, duration*
Are Mitigations Identified in Report: □YES. □NO **What is the proposed Mitigation Class** *Final mitigation class will be determined by SAG with concurrence of PRIME and USAID. Attach Mitigation Plan for class 2 and 3 mitigations (Mitigation definitions Appendix) 4*

General Project Description: Provide a *brief description (200 words or less) of the project. This should be a brief high-level description of the project development effort and its goals. This description is intended to inform/familiarize the SAG with the project they are about to evaluate. From report to report this section may only receive minor modifications as development progresses.*

Summary of Milestones and Benchmarks for the Reporting Period (from XX to YY)

Milestone, Benchmark or Go/ No-Go Criteria	Description	Description of Progress/Proposed Mitigation Class, if relevant	Completion date Actual/Revised	Comments

In tabular format, identify each milestone, benchmark or Go/ No-Go criteria from the Work Plan that was scheduled for completion in the 6-month reporting interval and provide a declarative statement describing its current status. If a research or administrative event occurred requiring mitigation for a specific milestone, benchmark, or Go/ No-Go criteria, pre-classify it with a mitigation code (Class 1, 2 or 3, Appendix 1, Definitions), briefly describe the proposed mitigation, its impact and prepare a mitigation report for class 2 and 3 mitigations to be attached to the MBR (Appendix 4). Class 1 do not require a report but should be described.

Examples of milestone, benchmark or Go/ No-Go criteria descriptions. There may be multiple milestones, benchmarks or Go/ No-Go criteria that are due in the reporting period. All should be included in the table..

Indicate whether Milestone, Benchmark or Go/ No-Go Criteria	Description	Description of Progress/Proposed Mitigation Class, if relevant	Completion date Actual/Revised	Comments

Milestone	*Complete 30-Day rat Safety study*	Ongoing	Proposed XXX	Ongoing with a Class 1 mitigation-waiting on CRO to start.
6-month Benchmark or Go/ No-Go	*Identify and audit CRO for Rat Study*	CRO chosen and audited	XXX	Audit confirmed quality processes in place. For GLP
6-month Benchmark or Go/ No-Go	*ACUC approval for study*	Approved	XXX	Protocol approved ready for implementation
6-month Benchmark or Go/ No-Go	*Begin Rat study*	Mitigation Class 1	XXX/XXX	*Waiting on CRO scheduling/ Class 1 mitigation—Potential 4 month delay---no action by Project team,*
6-month Benchmark or Go/ No-Go	*Provide Study Product to CRO*	*Delay of approximately 5 months, GMP manufacturer failed to meet final specification on study project of viscosity- Class 2 mitigation*	XXX/XXX	*Appears to be a stirring problem, GMP manufacturer has identified a fix and is remaking the study product. Projected completion date XXX*

If a milestone, benchmark, or Go/ No-Go criteria class 3 mitigation is identified report it as above and prepare a mitigation report.

Budget Status

On budget ___ Underspending ___. Overspending ____

If there are modifications to the budget as a result of mitigations and/or anticipated needs, please provide a revised budget in Appendix 3.

For Critical Path (CP) Projects Only: Is off ramping to Domain 2 of the Technology Accelerator requested?

If YES, briefly describe (250 words or less) the component proposed for off-ramping**?**

Identify if all or a portion of the CP is requested to be off-ramped. Provide a justification for the off-ramping and whether On-ramping back to the CP is anticipated and when.

<u>Progress</u> Narrative (1 Page)

Provide a brief specific narrative of data obtained, or studies done. This is a concise narrative of the work done in the reporting period and its relationship to the goals of the CP or Technology Accelerator project. Data may be included. Tables and legends may not be smaller than 10 point font and all figures and figure legends should be legible t 150% magnification (MS WORD). Margins must be 1 inch.

***Appendix 2** may be used to provide additional information to support statements in the narrative. The appendix may be no longer than five (5) pages. If the Appendix is used to provide supporting data for the Progress narrative, the data in the Appendix should be hyperlinked to the statements in the Narrative.*

The SAG is under no obligation to read the Appendix.

SAG Recommendation:

To be filled out by the PRIME after concurrence of USAID with the SAG recommendations. The recommendation will include the evaluation of the Mitigation Plan, if appropriate.

Additional SAG Recommendations

End of page

Appendix 1: Mitigation Class Definitions

See full description of the mitigation classes and process in the SAG charter

Class 1: Minor or transitory delays in research.

- The resolution of Class 1 mitigation issues is in general out of the hands of the PDL.
- No separate mitigation Report required.
- The resolution of the mitigation issue is reasonably expected to take no more than 6 months or 1 SAG reporting interval.

  Examples of this type of mitigation are timing of animal studies by CROs, delays in IACUC or IRB approvals, natural disaster delays, PDL institutional administrative delays, regulatory delays, etc. In this case, the PDL will place an explanation of the delay in the MBR report and provide a projected best- and worse-case resolution scenario, timeline, as well as alternatives, if any (e.g., alternative source or CRO) to resolve the issue if it cannot be resolved in the SAG reporting interval.

Class 2 : Moderate Delays in Research.

- Adverse finding where a resolution of the issues encountered are possible within a limited time frame that will not impact overarching milestones (i.e., clinical testing in 4 years) benchmarks and Go/ No-Go criteria but require a focused research effort to keep the R&D process on track.
- A mitigation report is prepared
- Class 2 Mitigations should be resolved as quickly as possible. It is expected that resolution of a Class 2 mitigation could take more than 6 months but are likely to be resolved in less than 12 months.

  Examples are minor modifications of formulations to meet stability requirements, need for a minor modification of a synthetic or manufacturing process, minor adjustments to formulations or delivery devices to meet desired/pre-defined rheological properties, etc.

- Because of the expected quick resolution of Class 2 mitigations, it is not expected that these mitigations will initiate immediate off-ramping to Technology Accelerator Domain 2. However, if mitigation efforts extend beyond 12 months, with the consent of the PRIME and USAID, the mitigation can be reclassified to a Class 3 and the project moved to Domain 2 of the Technology Accelerator.

Class 3: A severe to catastrophic problem/delay in product development

- Could potentially halt development (fatal flaw in drug substance or drug product) or delay development for an extended period of time (>12 months), resulting missed milestones, benchmarks and Go/No-Go criteria.

- A mitigation report is prepared

  Examples are failure of a stability program that indicates major changes are needed in the formulation or API, a serious safety finding or adverse event in preclinical or clinical studies, respectively, failure of GMP manufacturing or meeting GMP quality requirements.

- A critical part of any Class 3 mitigation will be a determination if all or part of the CP project requiring mitigation needs to be off ramped to Technology Accelerator Domain 2 and whether other activities within the CP should continue, with or without modification. The PDL should identify parts of the CP that should continue as planned The SAG will recommend off-ramping and whether other activities in the CP should be continued. USAID will determine if these recommendations are followed.

Appendix 2: Supplemental Information

Page limit 5 pages.

The SAG is under no obligation to read the Appendix and it is provided to allow the product developer to expand on statements made in the 1-page project narrative section.

All data provided in the Appendix must be hyperlinked to the appropriate part of the Project Narrative for the convenience of the SAG.

All text must be in 12 pt times new Roman and Figures cannot use fonts smaller than 10 pt. The document must be readable as a paper copy to accommodate all possible modes of SAG member evaluation, electronic or paper.

Appendix 3: Budget Modifications

If changes are required to the budget based on the MBR prepare a dual column budget that indicates the original budget and the modified budget.

Item	Original Budget	Revised Budget	Justification

Appendix 4: Mitigation Plan

This Appendix is only used if there is a mitigation plan required to address adverse findings in the MBR. Mitigations plans are only required for Class 2 and 3 mitigations

See Mitigation Plan Template SAG Charter

Appendix 5: Project Descriptor *(required by USAID)*

Paste the 2-page project descriptor submitted for the MATRIX application into this section.

If the project descriptor requires updating mark changes in Red

Leave the red changes from previous MBR reports, unless directed to remove by the PRIME or USAID

Appendix 6: Gantt Chart *(required by USAID)*

Paste the Gantt submitted for the MATRIX application in this section.

If the Gantt Chart requires updating mark changes in Red

Leave the red changes from previous MBR reports, unless directed to remove by the PRIME or USAID

Appendix 7: TTP *(required by USAID)*

Paste the 2-page TPP submitted for the MATRIX application in this section.

If the TPP requires updating mark changes in Red

Leave the red changes from previous MBR reports, unless directed to remove by the PRIME or USAID

Appendix: 8 USAID Microbicides R&D Assessment *(required by USAID)*

The USAID Microbicides R&D Assessment should be reviewed and updated by the development team prior to each biannual SAG meeting. If new information has been obtained that allows you to provide additional or updated information, make those changes and indicate them in Red. When filling out the next MBR remove previous Red change indicators.

Appendix 4: Mitigation Plan Template Mitigation Report for Class 2 and 3 Mitigations

Mitigation Plan Template Mitigation Report for Class 2 and 3 Mitigations

MDR reports must be in Microsoft Word with 12-point Times new Roman Font. All margins should be set a no less than 1 in. and must include the document headers and footers. Figures should be legible with no more than 150% magnification in MS Word. Reports that do not conform with formatting requirements and/or page and word limits will be returned as non-compliant

Date: *Date of SAG meeting*
Group/organization:
Product: *Drug/delivery system, duration*
Proposed Mitigation Class *(Class definitions MBR Appendix 1), Final mitigation class will be determined by SAG with concurrence of PRIME and USAID.*

Briefly list and describe (250 words or less) any other ongoing Mitigation activities for this CP or Domain 2 project.

Briefly list and describe any ongoing class 2 and/or 3 mitigations and how this mitigation request relates to the previously approved mitigation plan(s). Specifically address the impact of the multiple mitigation plans on each other. Is resolution of one plan continent on the success of the other? Briefly quantify the impact of this plan on project timelines, identify whether this plan will result in significant changes to the project plan s Gantt chart, TPP, Milestones, benchmarks and Go/ No-Go criteria.

Indicate the projected time required to complete the mitigation activities.

Provide a projected project duration for the mitigation plan. Provide both best case and worse case estimations. Identify whether the time to resolution is dependent upon factors out of control of the product developer, i.e., requires IRB, IACUC or other administrative/regulatory approvals to implement.

For Class 3 mitigations only, are you requesting approval to off-ramp all or part of the Critical Path Project (CP) to Domain 2 of the Technology Accelerator?

If the answer is no, move to the next question. If the answer is yes, identify whether all or a part of the critical path project will be off-ramped. If only a part, in the table below list the activities and associated milestone, benchmark or Go/ No-Go criteria associated with the components to be and not to be off ramped.

CP Activity	Milestone, Benchmark, Go/No-Go criteria*	Off-Ramping Yes/No	Comments

**Milestone, benchmark, Go/ No-Go associated with the CP activity.*

Describe the Mitigation Plan (500 words or less).

Describe the issue(s) to be mitigated and how it will be mitigated. Indicate how the mitigation plan will resolve the issues encountered.. Describe the experimental design to be used and the expected outcomes, where appropriate.

Multiple mitigations that are interrelated (e.g., redesign a formulation and perform stability testing) can be described in the same description. If they are multiple mitigations describe provide a mitigation classification for each.

In Appendix 1 Provide a Gantt chart, and Timeline for the Mitigation Plan (2 pages).
Identify the any relevant dependencies in the Gantt Chart and indicate critical milestones, benchmarks, and Go/ No-Go criteria in the timeline

Describe a Successful Mitigation and the Decision Points for Determining a Successful Mitigation (200 words or less)
What needs to be accomplished to return to the CP? What Milestones, Benchmarks, Go/ No-Go criteria must be met to signal a successful mitigation. If you are requesting off-ramping to Domain 2, what criteria need to be met to return to the CP.

Does the need for or the outcomes of the mitigation plan result in changes in the CP project descriptor, Gantt Chart, TPP or USAID Microbicide R&D Assessment?

If yes which appendices were modified.

Modify the appropriate documents in the appendices of the MBR, following the instruction in the Appendices for each component
Appendix 5: Project Description
Appendix 6: Gantt Chart
Appendix 7: TPP
Appendix 8: USAID Microbicide R&D Assessment

Describe Futility (150 words or less)
Provide a 150 word or less discussion of what futility would look like. Futility is defined as the inability to mitigate the identified problem sufficiently to continue with the planned CP project.

Projected time to complete the mitigation.
Best Case Scenario: *Days or date*
Worst Case Scenario: *Days or date*
Provide a best- and worst-case scenario for completion of the proposed mitigation plan. These times should be reflective of the Gantt Chart and Timeline provided in Appendix 6.

Mitigation Plan Budget
Provide a brief (200 words or less) narrative of the budget required for the mitigation, its impact on the CP, and how it will be obtained. A more detailed budget will be provided in Appendix 2.

Indicate whether rebudgeting will be sufficient to complete the mitigation plan or if new funding is anticipated to be needed. Indicate the amounts of to be rebudgeted or new funds to be requested.

Indicate whether budgeting will create a shortfall in future activities and whether that shortfall can be met by rebudgeting other CP activities in out-years.

If other CP activities will be ongoing during the Mitigation plan implementation describe any potential impact on these studies.

SAG Recommendation
To be filled out by the PRIME after concurrence of USAID with the SAG recommendations. The SAG may recommend a variety of outcomes for the Mitigation plan. They may recommend proceed as planned,

recommend off-ramping to Domain 2 of the Technology Accelerator (not requested in the plan) or may recommend futility for the CP project based on the severity of the mitigatable issue. In all cases, the mitigation plan will not be officially implemented until concurrence is received from USAID.

Additional SAG Recommendations

Appendix 1: Gantt chart and timeline for the Mitigation Plan

Two (2) pages.

Gantt chart and timeline formatting should follow original document fonts and sizing submitted with the MATRIX application

Identify any relevant dependencies in the Gantt Chart and indicate critical milestones, benchmarks, and Go/ No-Go criteria in the timeline.

Appendix 2: Mitigation Plan Budget

Provide a detailed budget for the mitigation. Indicate where the funds for the mitigation are coming from and any shortfalls or reduction in scope the new budget will create for the CP.

Appendix 5: New Project Requests

Submission of new project requests must be preceded by an invitation by the MATRIX PRIME with USAID concurrence to submit. Permission to submit a new project request does not imply approval to start the project.

New Project Requests must be in Microsoft Word with 12-point Times new Roman Font. All margins should be set a no less than 1 in. and must include the document headers and footers. Figures should be legible with no more than 150% magnification in MS Word. Reports that do not conform with formatting requirements and/or page and word limits will be returned as non-compliant

New Project Identifier

The new project identifier should describe the product or activity to be conducted in the new project, i.e., Development of XXX drug for long-acting HIV prevention, Development of a highly sensitive point of care measuring device, Development of a novel in situ detection method for implanted long-acting HIV prevention strategies, etc.

Date: *Date of submission of the new project request to MATRIX*
Date Of Invitation to submit a new project request: *Date New Project approved for submission to the SAG.*

Date of Scientific Advisory Group (SAG) Evaluation:

Group: *Entity submitting the request. Can be an individual investigator, lab, or institution. New projects maybe proposed by SSA investigators, investigators already in MATRIX or invited investigators.*

Relationship to Matrix:

External to MATRIX/Internal to MATRIX, residing in the US, SSA or other.

Type of Project Request:

Indicate whether the new project is proposing on-boarding of a new Critical Path (CP) project or new Domain 1 Technology Accelerator project.

This form may also be used to propose a new Technology Accelerator Domain 1 project for a CP or Domain 2 Technology Accelerator project that has been terminated. The elements eligible for this later type of new project onboarding are highly innovative activities within the terminated parent project that the MATRIX PRIME and USAID wish to continue. PRIME with USAID concurrence will decide the scope of the new project and invite the new project submission.

USAID Priorities addressed: (100 words)

Describes how the new project address the overarching USAID activities of developing long-acting HIV prevention strategies or multipurpose prevention technologies (MPT) that are acceptabile, affordable, scalable and /or deliverable. Ideally new projects will incorporate attributes that enable each of the 4 product factors; however, Technology Accelerator Domain 1 projects maybe focused on enhancing a single factor for the HIV prevention field in general though development or testing of a critical process or capability.

Identify the HIV at-risk population(s) that the new project will serve.

If the new project is being used to mentor (new or existing) or create/increase infrastructure capacity for SSA partners, identify the partners and what the partner will gain from the new project or how the projected impact of the new infrastructure. A more in-depth description will be provided in **New Human Capital** below.

Proposed Duration of Project:

For all new projects, the performance period can be no longer than the base MATRIX award (November. 30, 2026). Ideally Domain 1 technology Accelerator projects will be completed in 6 to 18 months.

Brief Description of the New Project:

Brief description (500 words or less) of the proposed new project.

Describe the proposed experimental design and identify critical milestones, benchmarks, and Go/ Go-Go Criteria if applicable.

Specific outcomes of the project should be described (see examples below)

- New CP Project. Filing a Pre-IND or first in human clinical testing of a novel insert novel HIV Long - acting HIV Prevention or MPT product/strategy.

- Domain 1 Technology Accelerator project: Proof of concept for the product, technology, or drug delivery device. Describe how the proof of concept advances the field of HIV prevention and USAID Prevention objectives.

Describe any New Human Capital Created by the New Project (100 words or less)

Will the project be part of a mentoring or training program for a Sub Sharan Africa investigator? Identify the investigators and institutions that will benefit from the new project and how it benefits USAID. What will the investigators gain from participating in the new project? Will the new project enhance existing or create new infrastructure in the labs or institution it is carried out in? What new infrastructure will be created, e.g., new methods and assays to test anti-HIV drugs?

Impact of New Project on MATRIX Goals *(200 word of less)*

Describe how the work fills a gap within MATRIX and add to the HIV prevention field by supporting MATRIX R&D. Provide sufficient reasoning for the activity to be brought on/into MATRIX.

For new projects derived from terminated CP or Domain 2 projects the impact statement must also identify the specific value of the "rescued" project to USAID and what resources will be lost if not approved.

New Project Timelines, Milestones, Benchmarks, Product Summary and TTP: Appendices 2-4 and 6.

Attach the appropriate documents in the appendices
Appendix 2: Timelines, Milestones and Benchmarks
Appendix 3: Product Descriptor (2 pages)
Appendix 4: Targeted Product Profile. (2 pages)

Only for New CP projects
Appendix: 6 USAID Microbicides R&D Assessment

The Definitions of Timeline, Milestone. Benchmarks and Go/ No-Go can be found in Appendix 1.

For new CP projects

The following documents are required:
2 Page milestone and benchmark Gantt chart Appendix 2
2 Page Product summary (Appendix 3) that discusses the following

1. *Pre-clinical/Clinical development plan*
    a. *Lead(s) drug substance (Active Pharmaceutical Ingredient(s) API(s))*
    b. *Drug delivery system*
    c. *Product manufacturing plans and options*
2. *Regulatory strategy and timing*
3. *Product cost evaluation- [tied to solution. 6]*
4. *Plans for key consumers/end-users' and stakeholders' input- [tied to solution 4]:*
    a. *Acceptability and user preference considerations*
    b. *Affordability, scalability, product delivery considerations*
5. *Status of technology and technical approach (include R&D benchmarks)*
6. *IP and patents considerations*
7. *Key risks and unknowns*
8. *Value added and relevance*

1 Page TPP Appendix 4
Fill out the USAID Microbicides R&D Assessment Appendix: 8

New Domain 1 Technology accelerator projects
Provide in Appendix 2 in tabular form milestones and benchmarks and a specific Go/No-Go criterion that will used to identify the completion of the technology accelerator project. A Product Summary (Appendix 3) and TPP (Appendix 4) are only needed if the Project is developing a Long-acting anti-HIV antiviral or MPT.

Budgets and personnel

Provide a budget as indicated in Appendix 5

New CP project require a detailed year 1 budget and a predicted total budget in subsequent years
Domain 1 projects will provide a detailed budget for the duration of the project.

SAG recommendation

To be filled out by the PRIME after concurrence of USAID with the SAG recommendations. The SAG may recommend approval or disapproval of the new project. In all cases, the new project will not be officially implemented until concurrence is received from USAID.

The SAG Review of new Domain 1 Technology Accelerator will be a courtesy review to familiarize the SAG C Committee with the project and to establish the required project documentation. The SAG will be asked if they concur with the proposed onboarding by The MATRIX Prime and USAID of the project.

Additional SAG Recommendations

Appendix 1: Definitions

Timeline: A chronological arrangement and identification of critical events in their order of occurrence during product development. Usually provided as a graphical representation of projected time and events.

Milestone: A research milestone is a measure of progress. Milestones identify critical junctures/steps in the research process that must be accomplished/completed in order to successfully complete the research. A milestone may also incorporate Benchmarks and Go/ No-Go criteria in its description as measures of progress in attaining the milestone.

Example of a Milestone: Complete Rat Safety and PK study

Benchmark: A point of reference that can be used to judge progress, usually toward a milestone. Benchmarks composed of the steps required to complete a project can be used to measure progress of the project.

Example of a Benchmark: Ro complete a Rat Safety and Pharmacokinetic study milestone the PI needs to identify a contract research organization (CRO) to perform the study, write a protocol, get IACUC approval for the protocol, make drug product to test, perform the study and analyze the study. Each of these steps could be identified as a benchmark, measuring progress toward the overarching milestone of performing the Rat Safety and Pharmacokinetic study.

Go/ No-Go Criteria: These are critical decision points stated as absolutes in the development pathway of a product. Go and No-Go can be applied to Milestones and benchmarks. Go is a decision to continue development. No-Go is a decision to stop development. A single milestone or benchmark may have multiple Go/ No-Go criteria depending upon its complexity. Passing a Go/No-Go gate (Go) allows the research program to proceed to the next milestone or benchmark.

Example of a Go and No-Go
Milestone complete Safety and Rat Pharmacokinetic study
Go: There are no safety issues and the prespecified pharmacokinetic parameters were met.
No-Go. There are safety concerns and/or the pharmacokinetic parameters were not met.

Appendix 2: Timelines Milestones and Benchmarks (2 pages)

For New Projects in Domain 1 Technology Accelerator provide a single Go/ No-Go Criterion to be used to measure completion of the project, e.g., GO: The new instrument will have sensitivity of XXX and selectivity of XXX; NO-GO Failure to meet sensitivity or selectivity criteria.

Appendix 3: Project Descriptor (2 pages)

Describe the proposed new project.

For new CP projects

The following documents are required:
2 Page milestone and benchmark Gantt chart Appendix 2
2 Page Product summary (Appendix 3) that discusses the following

1. *Pre-clinical/Clinical development plan*
    a. *Lead(s) drug substances/ API(s)*
    b. *Drug delivery system*
    c. *Product manufacturing plans and options*
2. *Regulatory strategy and timing*
3. *Product cost evaluation- [tied to solution. 6]*
4. *Plans for key consumers/end-users' and stakeholders' input- [tied to solution 4]:*
    a. *Acceptability and user preference considerations*
    b. *Affordability, scalability, product delivery considerations*
5. *Status of technology and technical approach (include R&D benchmarks)*
6. *IP and patents considerations*
7. *Key risks and unknowns*
8. *Value added and relevance*

1 Page TPP Appendix 4
Fill out the USAID Microbicides R&D Assessment Appendix: 8

New Domain 1 Technology accelerator projects

Provide in Appendix 2 in tabular form Milestone and benchmarks and a specific Go/No-go criterion that will identify the completion of the technology accelerator project. A Product Summary (Appendix 3) and TPP Appendix 4 are only needed if the Project is developing a Specific Long-acting anti-HIV antiviral or MPT.

Appendix 4: TPP (2 pages)

The TPP should be in tabular format and contain the following elements

	Item	*Preferred Target*	*Minimum Target*
1	*Primary Indication*		
2	*Other indication(s)*		
3	*Target population*		
4	*Anticipated clinical efficacy*		
5	*Preparation*		
6	*administration /removal*		
7	*Safety, tolerability*		.
8	*Contraindications*		
9	*Product attribute/s*		
10	*Dosing frequency*		
11	*Disposal/waste*		
12	*Drug product shelf life*		
13	*Distributor storage conditions*		
14	*Packaging*		
15	*Regulatorystrategy*		
16	*Anticipated post licensure COGs for 1 person/year*		

Appendix 5: Budget

Provide a detailed first year budget of personnel, equipment, and reagents to conduct the new project. If the new project spans more than 1 year provide a total predicted cost for the year.

Appendix 6: USAID Microbicides R&D Assessment

This report will only be required for onboarding of new CP projects