MATRIX Clinical Trials Hub Procedure: Clinical Research Site (CRS) Selection

Standard Operating Procedure (SOP)#: CTH001, Version 1
Effective Date: 03/22/2023

1.0 Purpose:

1.1 To establish and describe the procedures for selecting clinical research sites (CRS) for participation in the MATRIX (Microbicide R&D to Advance HIV Prevention Technologies through Responsive Innovation and eXcellence) Collaborative's clinical research protocols.

2.0 Scope:

2.1 This procedure is applicable to all clinical research protocols (active and/or placebo product) implemented within MATRIX.

3.0 Authority:

U.S. Agency for International Development (USAID)
U.S. President's Emergency Plan for AIDS Relief (PEPFAR)
U.S. Food & Drug Administration (FDA)
Microbicide R&D to Advance HIV Prevention Technologies through Responsive Innovation and eXcellence (MATRIX)

4.0 References: (Check for the most up-to-date version of the following)

4.1	2 CFR Part 200	*Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards*
4.2	22 CFR Part 225	*Protection of Human Subjects*
4.3	USAID Automated Directives System (ADS) Chapter 201	*Program Cycle Operational Policy*
4.4	USAID ADS Chapter 303	*Grants and Cooperative Agreements to Non-Governmental Organizations*
4.5	ICH E6 Standard	*Good Clinical Practice (GCP)*
4.6	MATRIX Policy	*Good Documentation Practice (GDP)*
4.7	MATRIX Policy	*Human Subjects Research*
4.8	MATRIX List of Definitions	

5.0 Definitions:

See *MATRIX List of Definitions*.

6.0 Responsibilities:

6.1 Clinical Trials Hub Co-lead Principal Investigators (PI)

6.1.1 Oversee development of study-specific Site Selection CRS Capacity Questionnaire.

6.1.2 Provide general oversight of site selection process.

6.1.3 Provide general oversight of process for updating Site Capacity Catalogue.

6.2 MATRIX Prime Program Manager

6.2.1 In collaboration with the Clinical Trials Hub Co-lead PIs, develop the study-specific Site Selection CRS Capacity Questionnaire based on the CRS Capacity Questionnaire template (see Attachment 1 for questionnaire template).

6.2.2 Manage communications/logistics related to site selection process:

6.2.2.1 Solicit sites' interest in study participation (see Attachment 2 for sample solicitation email).

6.2.2.2 Collect materials from applicant sites and notify MATRIX leadership of interested sites.

6.2.2.3 Request addition of Site Selection vote to Steering Committee (SC) call agenda.

6.2.2.4 Distribute materials from applicant sites to SC members.

6.2.2.5 Collect Site Selection votes and, if applicable, "abstain" declarations from SC members.

6.2.2.6 Notify MATRIX leadership of voting totals.

6.2.2.7 Notify Protocol Team and Prime of site selection decision. Protocol Teams initially consist of Product Developer and USAID representatives, investigators and study coordinators from the newly selected sites, and members of the Clinical Trials and Design to Delivery Hubs.

6.2.3 Update Site Capacity Catalogue as needed, in collaboration with Clinical Trials Hub Co-lead PIs.

6.2.4 Save all CRS application materials, voting ballots, and other relevant documentation according to MATRIX's Good Documentation Practice (GDP) Policy.

6.3 MATRIX Product Developer Partners

6.3.1 Provide MATRIX Prime and/or Clinical Trials Hub staff with a protocol concept document that gives a brief synopsis of their planned clinical research protocol.

6.3.2 Provide additional guidance to SC members regarding preferred site characteristics for specific studies during the SC call discussion prior to Site Selection vote.

6.4 MATRIX Steering Committee (SC) Members

6.4.1 Review completed Site Selection materials from interested sites prior to scheduled Site Selection vote.

6.4.2 Discuss merits of applicant sites during the SC call.

6.4.3 Submit voting ballots or, if applicable, "abstain" declarations prior to or after the SC call.

6.5 MATRIX Executive Director and/or Deputy Director

6.5.1 Moderate site selection discussion and voting during the SC call.

6.5.2 Notify MATRIX Prime Project Manager (via email or on a call) of site selection decision.

6.5.3 Notify SC members of site selection decision at next scheduled SC call following the site selection vote.

6.6 Clinical Research Site (CRS) Personnel

6.6.1 Complete study-specific Site Selection CRS Capacity Questionnaire.

6.6.2 Send completed questionnaire and other materials to MATRIX Prime Program Manager.

7.0 Procedure:

NOTE: All MATRIX clinical research plans, including clinical research protocol concepts, are pre-approved by USAID through their Workplan approval process. USAID will review protocol concepts and any feedback provided will be incorporated into the protocol as appropriate.

7.1 Develop Study-specific Clinical Research Site (CRS) Capacity Questionnaire

7.1.1 Once a protocol concept is received from a MATRIX Product Developer partner, the MATRIX Prime Program Manager, in collaboration with the MATRIX Clinical Trials Hub co-lead PIs, develops a Site Selection CRS Capacity Questionnaire listing the specific site requirements and qualifications considered necessary for successful study implementation (see Attachment 1 for questionnaire template).

7.1.1.1 Study-specific site requirements and qualifications are developed by reviewing the approved protocol concept and any recommendations received from the MATRIX SC and/or Product Developer investigator(s) who proposed the concept.

7.1.1.2 Study-specific Site Selection CRS Capacity Questionnaires may omit items previously asked as part of Site Capacity Catalogue development and/or previous protocols' site selection processes.

7.1.2 Example site selection criteria include:

7.1.2.1 Training and experience of the lead investigator(s) at the site(s), potential access to the designated study population(s), previous experience and performance in conducting early stage and placebo studies, laboratory capacity, pharmacy capacity, sample storage capacity, infrastructure for regulatory compliance and oversight, etc.

7.2 Send CRS Capacity Questionnaire to Partner Sites and Solicit Interest in Study Participation

7.2.1 The MATRIX Prime Program Manager or designee sends an email to the designated representative(s)/contact(s) from each eligible MATRIX partner CRS as defined by the protocol concept or the MATRIX SC.

7.2.1.1 The email includes the Protocol Concept and Site Selection CRS Capacity Questionnaire, and requests that sites submit the completed questionnaire and accompanying documents via email to the MATRIX Prime Program Manager or designee by a specific deadline (see Attachment 2 for sample solicitation email).

7.3 Interested Sites Respond to Call for Sites

7.3.1 Site personnel complete the Site Selection CRS Capacity Questionnaire and return the scanned copy of the completed/signed/dated document and any accompanying documents via email to the MATRIX Prime Program Manager or designee before the specified deadline.

7.4 Notify MATRIX Executive Director and Deputy Director of Applicant Sites

7.4.1 Once the deadline for application is met, the MATRIX Prime Program Manager or designee notifies (via email or on a call) the MATRIX Executive Director, MATRIX Deputy Director and Clinical Trials Hub co-lead PI of which sites applied for participation.

7.5 Add Site Selection Vote to MATRIX SC Agenda

7.5.1 The MATRIX Prime Program Manager or designee requests (via email or on a call) that "Site Selection" be added to the next MATRIX SC meeting agenda and creates a study-specific ballot for the site selection vote (see Attachment 3 for voting ballot template).

7.6 Distribute Site Selection Review Packet to MATRIX SC Members

7.6.1 The MATRIX Prime Program Manager or designee creates and distributes a packet to all MATRIX SC members via email prior to the next MATRIX SC meeting.

7.6.1.1 The packet includes copies of the protocol concept, all completed Site Selection CRS Capacity Questionnaires and accompanying documents, and one blank Site Selection Voting Ballot.

7.6.2 The MATRIX Prime Program Manager or designee then saves a copy of the packet and a record of recipients according to MATRIX's GDP Policy.

7.7 Mitigate Conflicts of Interest (CoI) among MATRIX SC Members

7.7.1 Prior to open discussion, any SC members whose sites are being considered for inclusion in a protocol are asked to leave the call and to abstain from voting.

7.7.1.1 SC members with a CoI complete the ballot by checking the "abstain" category, and their vote is listed as "abstain" in the final tally of votes collated by the MATRIX Prime Program Manager or designee.

7.8 Discussion during MATRIX SC Meeting and Voting

7.8.1 Discussion by MATRIX SC members and USAID representatives attending the SC call takes into consideration each applicant site's past performance on previous studies,

information previously provided for the MATRIX Site Capacity Catalog, and their written responses in the Site Selection CRS Capacity Questionnaire.

7.8.2 MATRIX SC voting members cast their votes using the provided ballot and submit it to the MATRIX Prime Program Manager or designee via email after the meeting.

7.9 Tally Votes and Establish Consensus

7.9.1 The MATRIX Prime Program Manager or designee tallies the ballot votes.

7.9.1.1 Reminder emails will be sent one week after site selection discussion to all SC voting members who have not yet submitted their ballots.

7.9.2 Once a quorum of the ballots has been received, the MATRIX Prime Program Manager or designee emails the results to the MATRIX Executive Director, MATRIX Deputy Director, and Clinical Trials Hub co-lead PI.

7.9.2.1 A voting quorum is defined as having received ballots from a majority of SC voting members, such that any outstanding ballot(s) would not affect the site selection results.

7.9.2.2 Quorum requirement may be waived if number of applicant sites equals the number of sites needed for the study.

7.9.3 The MATRIX Prime Program Manager or designee then saves the completed ballots, tallies and other relevant documentation according to MATRIX's GDP Policy.

7.10 Announce Site Selection Decision(s)

7.10.1 Upon receiving confirmation from the MATRIX Executive Director and/or Deputy Director, the MATRIX Prime Program Manager or designee sends an email to the Protocol Team, copying the Prime, notifying them of the voting results (see Attachment 4 for sample site announcement email).

7.10.1.1 Protocol Teams initially consist of Product Developer and USAID representatives, investigators and study coordinators from the newly selected sites, and members of the Clinical Trials and Design to Delivery Hubs.

7.10.2 The MATRIX Prime Program Manager or designee then saves copies of the email notification according to MATRIX's GDP Policy.

7.10.3 The MATRIX Executive Director or MATRIX Deputy Director notifies SC members of the voting results at the next scheduled SC call following the site selection vote.

7.11 Update Site Capacity Catalog

7.11.1 The MATRIX Prime Program Manager, in collaboration with the Clinical Trials Hub co-lead PIs, updates the MATRIX Site Capacity Catalog to reflect sites' responses to the Site Selection CRS Capacity Questionnaire.

7.11.1.1 Updates to the Site Capacity Catalog will be compiled and incorporated into future Catalog versions on an annual basis.

8.0 Document History

Version / Date Effective	Summary of Changes	Revised by / Approved by
A / [*03/22/2023*]	Original Release	L. Duran / N. Mgodi / S. Hillier

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9.0 Approvals

DocuSigned by:
Luis Duran
Signer Name: Luis Duran
Signing Reason: I am the author of this document
Signing Time: 7/25/2023 | 8:24:53 AM PDT
4F4E4A7E27804D9387497FBC68D468A2

Prime Program Manager Signature — 7/25/2023 — *Date (month/day/year)*

DocuSigned by:
Nyaradzo Mgodi
Signer Name: Nyaradzo Mgodi
Signing Reason: I approve this document
Signing Time: 7/25/2023 | 1:19:47 PM PDT
CA2EE955FFE04C83BFE4F075EC10A21E

Clinical Trials Hub co-lead PI Signature — 7/25/2023 — *Date (month/day/year)*

DocuSigned by:
Sharon Hillier
Signer Name: Sharon Hillier
Signing Reason: I approve this document
Signing Time: 7/25/2023 | 8:28:46 AM PDT
437BF8C12B1541729992EA42A322B571

Executive Director's Signature — 7/25/2023 — *Date (month/day/year)*

Clinical Research Site (CRS) Capacity Questionnaire: Site Selection

MATRIX-[*XXX*]

[*Insert Study Title*]

Instructions: If you wish to apply for your site to participate in MATRIX-[*XXX*], complete this questionnaire, print the completed questionnaire, hand sign and date it, **scan the completed, signed, dated questionnaire and email it to [*XXX*]** by the date noted in the solicitation email.

1. Name and physical address of your Clinical Research Site (CRS):

    a. Please provide specifics about your CRS's hours of operation during MATRIX-[XXX] (i.e., [*expected dates of study duration*]). Please specify evening/weekend hours, days of the week, etc.

2. Name(s), email(s), phone number(s) and current biosketch(es) (within 2 years; please attach to questionnaire) of CRS Lead Investigator(s):

3. Names, emails, phone numbers and current biosketches (within 2 years; please attach to questionnaire) of CRS clinician(s) and coordinator(s) who will have a leadership role in MATRIX-[XXX], if different from above:

4. Why do you want to participate in MATRIX-[XXX]? (Maximum 100 words)

5. Do you have access to the study population described in MATRIX-[XXX] (i.e., [*description of target study population*])?

6. Study participants must be [*compliant with or willing to comply with key study inclusion/exclusion criteria, e.g., use contraception, remain sexually abstinent, etc., and/or willing to be randomized to placebo product*]. What challenges, if any, do you foresee regarding recruiting participants who [*are already compliant with and/or would be willing to comply with criteria, e.g., initiate contraception, remain sexually abstinent, be randomized to placebo, etc.*]? Please describe how you would address these challenges.

7. Please characterize the contraceptive use profile of the MATRIX-[XXX] target population (i.e., [*description of target study population*]) in your area. This could include contraceptive prevalence, methods available and methods used.

Clinical Trial and Investigator-Driven Research Experience/Capacity

[*Include questions #8-15 as applicable depending on study population and type of study*]

8. Do you have previous experience conducting first-in-human (FIH) or Phase 1 acceptability/tolerability studies?

YES **NO** If "Yes", please list below:

Study Number and Full Name/Descriptor	**Product**	**No. of participants screened/enrolled**

For the studies listed above, please describe strategies used for recruiting and retaining participants and note which strategies were most successful.

9. Do you have previous experience conducting pharmacokinetic (PK) studies?

YES **NO** If "Yes", please list below:

Study Number and Full Name/Descriptor	**Product**	**No. of participants screened/enrolled**

For the studies listed above, please describe strategies used for recruiting and retaining participants (if different from those described previously) and note which strategies were most successful.

10. The schedule for PK sample collection requires participants to be seen on [*PK sample collection visit schedule for study*]. Would you be able to see participants on that schedule? Please provide specifics on how your CRS would accommodate participants on that visit schedule.

11. Does your clinic have the ability to collect cervicovaginal tissue biopsies? If yes, please describe; if no, please describe what you would need in terms of training, equipment, etc. for your clinic to have this ability.

    a. Do you have access to a laboratory that can conduct the following tissue sample analyses planned for MATRIX-[XXX]? Check all that apply:

    □ [*Tissue sample study endpoint #1*]
    □ [*Tissue sample study endpoint #2*]
    □ [*Tissue sample study endpoint #3…]*

12. Do you have previous experience conducting clinical studies evaluating only placebo products?

    YES **NO** If "Yes", please list below:

Study Number and Full Name/Descriptor	**Product**	**No. of participants screened/enrolled**

For the studies listed above, please describe strategies used for recruiting and retaining participants (if different from those described previously) and note which strategies were most successful.

13. Do you have previous experience conducting [*vaginal/rectal/multicompartment*] microbicide studies?

    YES **NO** If "Yes", please list below:

Study Number and Full Name/Descriptor	**Product**	**No. of participants screened/enrolled**

For the studies listed above, please describe strategies used for recruiting and retaining participants (if different from those described previously) and note which strategies were most successful.

14. Do you have previous experience conducting clinical trials of investigational contraceptive products/drugs?

YES **NO** If "Yes", please list below:

Study Number and Full Name/Descriptor	**Product**	**No. of participants screened/enrolled**

For the studies listed above, please describe strategies used for recruiting and retaining participants (if different from those described previously) and note which strategies were most successful.

15. Do you have previous experience conducting clinical studies with adolescent girls and young women (AGYW)?

YES **NO** If "Yes", please list below:

Study Number and Full Name/Descriptor	**Age Range of Study Participants**	**Product**	**No. of participants screened/enrolled**

For the studies listed above, please describe strategies used for recruiting and retaining participants (if different from those described previously) and note which strategies were most successful.

Social and Behavioral Research (SBR) Experience/Capacity

[*Include questions #16-18 as applicable depending on study objectives/endpoints and planned behavioral assessments*]

16. Do you have previous experience conducting early phase clinical studies that incorporate [*planned quantitative behavioral assessments, e.g., questionnaires re: drug/product acceptability, preferences, etc.*]? List most recent three.

YES **NO** If "Yes", please list below:

Study Number and Full Name/Descriptor	**Method(s) Utilized**	**No. of participants screened/enrolled**

17. Do you currently have the ability to administer [*planned quantitative behavioral assessments*] using any of the following tools? Check all that apply; if yes, please describe; if no, please describe what you would need in terms of training, equipment, etc. for you to have this ability:

□ Web/cloud-based applications (e.g., REDCap)

□ Audio / Computer-assisted survey instruments (A/CASI)

□ Text messaging (SMS) or other remote applications (e.g., WhatsApp)

18. Do you have previous experience conducting early phase clinical studies that incorporate [*planned qualitative behavioral assessments, e.g., in-depth interviews [IDI], focus group discussions [FGD], key informant interview [KII], discrete choice experiments [DCE], participant-centered counseling, etc.)*]? List most recent three.

YES **NO** If "Yes", please list below:

Study Number and Full Name/Descriptor	**Method(s) Utilized**	**No. of participants screened/enrolled**

Community Engagement Capacity

19. Describe your community advisory board (CAB) composition in terms of [*demographic and/or other characteristic(s) relevant to target study population*].

20. How do you plan to engage the local community(ies) and stakeholders in preparation for MATRIX-[XXX], during implementation and at results dissemination?

Participant Recruitment/Retainment Capacity

21. What other studies do you expect would run concurrently with MATRIX-[XXX] at your site during [*study implementation year(s)*]? Would any of those studies be drawing from a similar population as MATRIX-[XXX]?

Study Number and Name	**Intervention /Product**	**Anticipated total enrolled from your site**	**How is the population similar?**	**Expected dates your site:** • **Begins screening** • **Completes enrollment** • **Completes follow-up**

22. Please comment on recruitment strategies you would likely employ for MATRIX-[XXX] (e.g., radio, SMS, community-based events, clinic-based advertisements, etc.) and specify by name the places and/or venues from which you might target potential participants for recruitment.

23. Please describe plans to engage and retain MATRIX-[XXX] participants, including possible services offered within the clinic, how staff might engage with them, what activities the participants might do while at the clinic, etc.

24. Please describe possible barriers to MATRIX-[XXX] participants attending clinic visits, such as schedules and transport, and how you would address these.

25. Please state the monthly enrollment rate you anticipate at your site (a range is acceptable).

Regulatory Experience and Capacity

26. Please list the regulatory approvals (including product importation and specimen transfer) required for MATRIX-[XXX] at your site (i.e., regulatory bodies, Ethics Committees, Drug Authorities, etc.).

27. How long do you anticipate it might take to obtain regulatory approval(s) (including product importation and specimen transfer) for MATRIX-[XXX]? What challenges, if any, would you anticipate in obtaining regulatory approval(s)?

28. What additional challenges would you anticipate in implementing MATRIX-[XXX] at your site? Identify any mitigation strategies you envision.

29. Briefly describe any recent (i.e., in the previous year) updates to risk mitigation procedures and/or disaster management plans at your site.

30. Does your site have any additional experience or expertise that you believe will contribute to conducting MATRIX-[XXX] successfully? (Maximum 100 words)

    This question is designed to provide you a place to add information not specifically requested already and/or explain what process(es) you plan to put in place for any response(s) you marked "No" above.

Signature Section

Please print your name and sign and date on the lines provided below.

_____
Printed Name of Person Completing this Questionnaire

_____ _____
Signature Date of Signature

MATRIX SOP #CTH001, Version 1, Attachment 2
MATRIX Site Solicitation Email Sample

NOTE: A Call for Sites email should include a brief description of the study (referring to an attached "protocol concept") and instructions for applying to participate, including a deadline for responses.

To: [*CRS leadership representatives from all potential applicant sites*]
Cc: [*MATRIX Prime, Clinical Trials Hub co-lead PI*]
Subject: Call for Sites to Participate in MATRIX-[*XXX*]

Dear MATRIX CRS partners,

The study concept document for MATRIX-[*XXX*], [*Insert Study Title*] is now available.

This MATRIX-[*XXX*] protocol is designed to [*Insert primary study objective*]. [*Insert brief description of study design, product(s) studied, and product use duration; also study population if not already included in study objective*]. Please refer to the attached protocol concept for further details about this interesting study.

I am writing today to solicit sites' interest to participate in this study and assess sites' capacity to implement this study successfully. If you are interested in participating in this study, please complete the attached MATRIX-[XXX] CRS Capacity Questionnaire and email a scanned copy of your responses and any accompanying documentation to [*MATRIX Executive Director, Deputy Director, Clinical Trials Hub co-lead PI, Prime Program Manager*] by close of business [*Insert deadline date*]. The MATRIX Steering Committee will review the applications and select sites at the next monthly meeting on [*Insert meeting date*].

Please feel free to contact me if you have any questions.

Best regards,

[*MATRIX Prime Program Manager*]

SITE SELECTION VOTING BALLOT

MATRIX-[*XXX*]
[*Insert Study Title*]

(Please RANK your selections below)
1 = First Choice; 2 = Second Choice, 3 = Third Choice, 4 = Fourth Choice, 5 = Fifth Choice

South African (SA) CRS

_____ Aurum Institute [*Specify which location*]

_____ Centre For the Aids Programme of Research in South Africa (CAPRISA) [*Specify which location*]

_____ Wits Reproductive Health and HIV Institute (Wits RHI)

Non-SA CRS

_____ Harare Health and Research Consortium (HHRC)

_____ Kenya Medical Research Institute (KEMRI)

_____ I abstain from voting due to a conflict of interest.

_____
Voting Steering Committee Member

MATRIX SOP #CTH001, Version 1, Attachment 4
MATRIX Site Announcement Email Sample

NOTE: A Site Announcement email should include a brief description of next steps in protocol development. The protocol version 0.1 template document should also be attached to this email.

To: [*Matrix-[XXX] Protocol Team members*]
Cc: [*MATRIX Prime*]
Subject: Protocol Template for MATRIX-[XXX], [*Insert Study Title*]

Dear MATRIX-[*XXX*] Protocol Team members,

I am pleased to announce that the following applicant sites – [*Insert sites*] – have been selected to take part in MATRIX-[*XXX*]. Welcome to the MATRIX-[*XXX*] Protocol Team!

Attached please find the protocol version 0.1 template for MATRIX-[*XXX*], [*Insert Study Title*], dated [*Insert date*]. The study-specific protocol template version attached has been adapted using [*Insert Product Developer*] protocol concept document dated [*Insert date*].

The MATRIX-[*XXX*] protocol will enroll approximately [*Insert brief description of study population, study objectives, study design, product(s) studied, and product use duration; also, key study restrictions if applicable*].

To ensure consistency across all MATRIX clinical research protocols, Clinical Trials Hub staff will perform a series of quality control (QC) checks on the MATRIX-[*XXX*] protocol document(s) prior to achieving Version 1.0. This is a requirement of all MATRIX clinical research protocols. Submission of Version 1.0 protocol document(s) to regulatory authorities prior to satisfactory completion of these QC checks will constitute a violation of MATRIX policies and procedures.

Therefore, we urge all MATRIX-[*XXX*] Protocol Team members to begin using the provided template version moving forward as we continue to draft the MATRIX-[*XXX*] protocol document(s). The attached template already incorporates all QC-relevant formatting requirements (e.g., document structure, cover page, table of contents, section headings, etc.). The template also includes recommended language (e.g., regulatory oversight, data management, clinical management, informed consent form, etc.) to address expected local regulatory approval requirements, including as relates to social and behavioral research in the context of early phase trials and placebo studies, without being overly prescriptive at this early stage of protocol development.

NOTE: Specific instructions/suggestions within the attached template document are identified with [*italicized brackets*].

Also note the Protocol Development Team email alias [*Insert email group address*] was created to facilitate communication and document sharing between MATRIX-[*XXX*] collaborators. It will become a valuable resource once regular team calls are established. We will send a Doodle poll next week to select a date/time for the weekly Protocol Development Team calls. We will also follow up by email next week with additional document review guidance.

If you have any questions, please do not hesitate to contact the Clinical Trials Hub at [*Insert email group address*].

Best regards,

[*MATRIX Prime Program Manager*]