MATRIX-007 Study-Specific Procedures (SSP) Manual Section 1 – Introduction, Site Activation, and Document Requirements

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1 Introduction

MATRIX is a five-year program funded by the U.S. Agency for International Development (USAID) in 2021 with a mission to expedite the research and development of HIV prevention products for women – including products designed to protect against both HIV and pregnancy – that in addition to being safe and effective, will be acceptable, affordable, scalable and deliverable in the settings where they are needed most. MATRIX is being implemented by Magee-Womens Research Institute (MWRI) in collaboration with nearly 20 partner organizations based in Kenya, South Africa, the United States and Zimbabwe. To achieve this goal, MATRIX work is divided under five activity hubs: Technology Accelerator, Clinical Trials, Design to Delivery (D2D), Business, Market Dynamics, and Commercialization Hub (BACH), and Capacity Strengthening, Engagement and Mentorship (CaSE). The MATRIX-007/CARE PrEP study [Safety Evaluation following Exposure to Cabotegravir-, Dapivirine- and Tenofovir-based PrEP during Pregnancy (CARE PrEP)] is conducted within the

Clinical Trials Hub (CTH); MWRI is the prime partner and serves as the study sponsor. For more information on the study management structure, see Section 2 (Study Structure and Oversight) of this study-specific procedures (SSP) manual.

This section specifies the sources of procedural information available to study staff, the responsibilities of the Country Principal Investigators (PI), and the process by which each country's study team will be approved to initiate implementation of MATRIX-007.

Each country's study staff members are responsible for the proper collection, management, storage, quality control, and quality assurance of all study-related documentation. This section also contains information on the essential documents that each study site must maintain throughout the study and as relates to establishing adequate and accurate participant research records for MATRIX-007.

1.1 Current Protocol Specifications

The table below documents the version history of the MATRIX-007 protocol and sample informed consent form (ICF), along with any Clarification Memoranda (CMs) and Protocol Amendments, if applicable, all of which are considered essential study documents. To ensure this section reflects the current specifications of the protocol, upon issuance of any future protocol CMs or Protocol Amendments, the table will be updated accordingly.

Table 1-1: MATRIX-007 Protocol History

Document	Date of document(s)
MATRIX-007 Protocol, Version 1.0 MATRIX-007 Sample Informed Consent, Version 1.0	3 JULY 2024

A CM will be utilized to make minor clarifications and/or corrections to the protocol; for example, a CM may be used to update or correct the protocol team roster or to correct minor errors and inconsistencies in the protocol. Institutional Review Board/Independent Ethics Committee (IRB/IEC) approval of CMs is not required by the sponsor; however, investigators may submit the CM to the IRB/IEC overseeing the study for informational purposes or, if required by local policies, for approval prior to implementation. CMs are effective immediately upon issuance to the protocol team.

Protocol Amendments will be used for changes to the protocol that result in the addition, removal, or modification of study information or procedures, including changes to the study design, objectives, eligibility criteria, procedures, data management/analysis plans, or sample Informed Consent form (ICF). Protocol Amendments will also incorporate content from any previously issued CMs. Protocol Amendments must be submitted to and approved by IRBs/IECs prior to implementation of the changes outlined.

Sites are expected to operate under the protocol version and associated amendments that are currently approved by the local IRB/IEC, as well as any CMs. Copies of all protocol documents should be made available to staff and maintained among site essential files. These documents are available on the MATRIX-007 webpage under Study Documents (https://www.matrix4prevention.org/activity-hubs/clinical-trials/matrix-007-care-prep/matrix-007-care-prep-study-documents).

In order to respond to emerging public health emergencies like the COVID-19 pandemic, sites may need to rapidly implement practices and procedures that are not in line with the protocol or SSP Manual (e.g., modified visit procedures in the interest of staff/participant safety, conduct of remote visits, etc.). Sites should communicate with the MATRIX-007 Management Team and document contingency plans related to the public health emergency proactively, to the best of their ability (and retrospectively, as needed).

For each visit where modifications due to public health considerations result in a deviation from the protocol, a single protocol deviation should be reported with the underlying reason (e.g., "COVID-19") written in the description field, followed by what was modified during the visit. As required, sites should communicate contingency plans and protocol deviations related to COVID-19 or other emerging public health emergencies to IRBs/IECs and other applicable regulatory bodies. Sites should keep all communications and documentation in the site essential document file.

1.2 Procedural Information

The MATRIX-007 study is guided by this SSP manual, which serves to supplement the MATRIX-007 protocol. It does not replace or substitute the protocol or its contents. In the event this manual is inconsistent with the information and guidance provided in the protocol, the protocol will take precedence. In the event study implementation questions are not adequately addressed by the protocol or this manual or if any inconsistencies between the two documents are identified, please notify the MATRIX-007 Leadership and Operations Group (LOG) at Management Team at matrix007LOG@lists.matrix4prevention.org. The LOG should also be consulted for general questions on protocol implementation or study procedures, including clinical assessments and/or data or case report form (CRF) completion procedures.

This group consists of the Protocol Co-Chairs, FHI 360 Clinical Research Manager and Data Management Research Associate.

Electronic versions of the SSP manual, the protocol, and all other study implementation tools will be made available to country Principal Investigators (PIs) and Study Coordinators (SCs) who are responsible for disseminating these materials and tools to all country team staff involved in the study prior to study implementation.

All study documents can be searched electronically for key words and phrases using the "find" keyboard function (CTRL+F). Sites are encouraged to become familiar with electronic searching to make specific guidance easier to locate in the study documents.

The protocol (CMs and amendments), SSP manual, and study materials issued by study management for reference or site-specific adaption will be posted to the MATRIX-007 webpage under Study Documents (https://www.matrix4prevention.org/activity-hubs/clinical-trials/matrix-007-care-prep/matrix-007-care-prep-study-documents).

1.3 Principal Investigator Responsibilities

MATRIX-007 must be conducted in accordance with the United States (US) Code of Federal Regulations (CFR) and the International Conference on Harmonisation Consolidated Guidance for Good Clinical Practice (ICH E6 GCP). In addition, MATRIX-007 must be implemented in accordance with all site-specific regulations, policies, and guidelines applicable to human subjects research in

general and/or the conduct of study procedures in particular. Copies of all such regulations, policies, and guidelines should be maintained in on-site essential document files.

Each Country PI must sign an Investigator Signature Form (protocol signature page [PSP]) and a MATRIX Investigator of Record (IoR) Form to formally indicate his/her agreement to conduct MATRIX-007 in accordance with the study protocol, applicable US regulations, and MATRIX policies. A copy of the PSP can be found in the MATRIX-007 protocol. A copy of the MATRIX IoR Form can be found in the MATRIX website (https://www.matrix4prevention.org/resources/regulatory-documents). A PSP must be signed by the PI for all initial protocol versions and all full protocol amendments. A MATRIX IoR Form must be completed by the PI prior to study initiation and updated as needed throughout the study (e.g., in case of changes to the sub-investigators, site locations or regulatory bodies listed on the form). The PI will provide copies of their signed PSP(s) and MATRIX IoR Form(s) to MATRIX CTH Regulatory (matrixregulatory@lists.matrix4prevention.org) and keep the originals on-site with their essential documents according to MATRIX's Good Documentation Practices (GDP) Policy (available at https://www.matrix4prevention.org/resources/matrix-policies).

The obligations and responsibilities assumed by the PI when signing the PSP and MATRIX IoR Form are listed on the forms themselves. Updates to the MATRIX IoR Form should be submitted to MATRIX CTH Regulatory (matrixregulatory@lists.matrix4prevention.org) with a short summary of any updates that were made.

All PIs are required to complete the MATRIX IoR training every 3 years (IoR training slides and training documentation form available at https://www.matrix4prevention.org/resources/regulatory-documents), prior to study initiation or prior to assuming responsibility for an ongoing study; documentation of this training should be filed in site essential documents. The PI may delegate his/her obligations and responsibilities for conducting MATRIX-007 to other qualified study staff members; however, delegation does not relieve the PI of his/her ultimate responsibility for all study procedures performed and all study data collected. Delegation of PI responsibilities must be formally documented on the country's Delegation of Duties (DoD) Log throughout study implementation. A template is available from the CRM.

A staff member may not fulfill the PIs role in the PI's absence. Full responsibility and authority over the protocol by anyone other than the PI may only take place if an additional MATRIX IoR Form that lists another person as the PI is completed and submitted to MATRIX CTH Regulatory (matrixregulatory@lists.matrix4prevention.org). Additionally, sites should notify the CRM and MATRIX CTH Regulatory of the change and complete any other documentation requested.

Staff regularly involved in the source documentation of endpoint data or those who are delegated to perform critical trial related procedures should be included on the MATRIX IoR Form as a sub-investigator. For MATRIX-007, such components may include, but are not limited to, primary/secondary endpoint assessment, collection of participant safety information, or confirmation of participant eligibility. For MATRIX-007, this will likely mean the country-based Study Coordinators and Clinical Research Assistants

It is critical that staff members have documentation of training and relevant qualifications prior to being delegated trial responsibilities. Training records should be well organized and consistent, and include versions, date of training, and full titles of documents being trained on. Staff names on training logs should match those on the DoD Log and other study records.

1.4 Financial Disclosure Forms

Country PIs, Protocol Co-Chairs and other lead/key study staff listed on the MATRIX-007 Protocol Team roster (i.e., MATRIX Prime/CTH, FHI 360, MOSAIC) must disclose any financial interests that may be affected by the outcome of the research or attest to the absence of relevant significant financial interests according to 42 CFR 50 prior to study involvement and annually thereafter until study end.

A blank 42 CFR 50 FDF is available on the MATRIX webpage (https://www.matrix4prevention.org/resources/regulatory-documents). All items can be entered electronically except for the signature and date, unless Docusign or similar electronic signature application is used. For more details, see MATRIX's Financial Disclosure and Conflict of Interest (FD-COI) Policy, available at https://www.matrix4prevention.org/resources/matrix-policies.

1.5 Site Activation Process

As MATRIX-007 is a multi-country, multi-site study, each site must be individually approved to conduct the study. It is anticipated that study activation will be staggered among countries and among sites within countries, as study activation requirements are unique to each site. Prior to undertaking any study procedures, each study site must complete the study activation process. Each stage of the study will require a separate activation approval.

All site activation requirements are outlined in the MATRIX-007 Site Activation Checklist. The country PIs and study coordinators (SCs) will work between site staff and relevant study management members to complete the checklists. The MATRIX-007 CRMs are responsible for tracking progress toward completion of activation requirements and signing (approving) checklists upon completion. After all activation requirements have been met, the CRMs will send email notification of approval to start. No protocol-specified study procedures may be undertaken at a site prior to receipt of the Site-Specific Study Activation Notice. The approval notification must be filed in essential documents.

1.6 IRB/IEC Submissions

Tables 1-2 and 1-3 list IRB/IEC submission and approval requirements pertinent to MATRIX-007. Table 1-2 lists the requirements that must be met PRIOR to study initiation. Table 1-3 lists the requirements that must be met DURING AND FOLLOWING study implementation. As needed, sites should engage relevant drug regulatory agencies (DRA) to review or acknowledge the MATRIX-007 protocol and related materials.

Country teams are encouraged to request that their IRBs/IECs acknowledge receipt of all documents submitted to them, and to request that the IRBs/IECs note both the effective date and the expiry date of all approvals. Procedures for IRB/IEC communications must be outlined in an SOP. Documentation of all correspondence with responsible IRBs/IECs (i.e., complete copies of all submissions, responses, and approvals) must be maintained in sites' essential files. Electronic copies of all documents should be stored in the relevant country-specific MATRIX-007 folder on the CARE PrEP SharePoint site. Original (source) paper documents should be filed at the country office in a secure location and scanned for electronic filing on SharePoint, as noted above.

Table 1-2: IRB/IEC Submissions Required Prior to Initiation of MATRIX-007

Documents to be submitted to IRB/IEC	Written Approval Required*
MATRIX Protocol, Version 1.0	Yes
ICFs: (English and local translations). *See SSP section 3 (Informed Consent) for a listing of required forms*	Yes
Country PI and other key investigators' current curricula vitae (CVs) and (if applicable) clinical license documentation	No
Country PI and other key investigators' current ethics and Good Clinical Practices (GCP) training certifications	No
Participant pre-screening, recruitment plans, and related materials (prior to use)	Yes
Other written information for study participants (prior to use)	Yes
Other documentation required/requested by the IRB/IEC, such as protocol implementation plans, standard operating procedures (SOPs), and data collection forms	If required by IRB/IEC

*Items marked "yes" are required by U.S. regulations and GCP guidelines.

Table 1-3: IRB/IEC Submissions Required During and Following MATRIX-007 Implementation

Documents to be submitted to IRB/IEC	Written Approval Required*
Study status reports/updates (per IRB/IEC requirements)	Yes
Protocol CMs (submission encouraged but not required)	No
Protocol Amendments resulting in a new protocol version	Yes
Amended ICFs (including forms that are amended due to Protocol Amendments as well as forms that are amended for site-specific reasons; e.g., to update participant incentive information or to update site contact information)	Yes
Reports of serious adverse events and social harms (per IRB/IEC requirements)	No
Protocol deviation (PD) reports (per IRB/IEC requirements)	No
Country PI current CV, ethics and GCP training certifications, and (if applicable) clinical license documentation (if country PI changes during the study)	No
Updated/additional participant recruitment plans and materials (prior to use)	Yes
Updated/additional written information for study participants (prior to use)	Yes
Other documentation required/requested by the IRB/IEC	If required by IRB/IEC
Final study report/closure report	No

*Items marked "yes" are required by U.S. regulations and GCP guidelines.

1.7 Study SOPs

Refer to the **MATRIX-007 Required SOP Content** document for an outline of topics that must be covered in SOPs. Teams may choose how to organize content in SOP documents by country and/or site level or by topic area. SOPs should be on the **MATRIX SOP Template** or approved institutional format.

Both documents are available in the MATRIX-007 webpage under Study Documents (https://www.matrix4prevention.org/activity-hubs/clinical-trials/matrix-007-care-prep/matrix-007-care-prep-study-documents).

Initial approval of all SOP documents by the CRM is required for site activation. Other relevant SOPs, tools, or other procedural documents required for study conduct will be outlined as relevant throughout the SSP manual.

These documents should be periodically reviewed during study implementation and updated as needed (e.g., annually or if procedures significantly change).

1.8 Participant Research Records

Study sites must maintain adequate and accurate participant research records containing all information pertinent to MATRIX-007 for each study participant. See Protocol section 11.1 and section 13.6 below for further information regarding all participant information which should be stored in locked file cabinets with access limited to authorized study staff.

The ICH E6 GCP defines the terms source data and source documentation as follows:

- The term **source data** refers to all information in original records and certified copies of original records related to clinical findings, observations, or other activities in a clinical study necessary for the reconstruction and evaluation of the trial (including all screening and enrollment). Source data are contained in source documents (e.g., original records or certified copies).
- The term **source document** refers to original documents, data, and records (e.g., hospital records; clinical and office charts; laboratory records and notes; memoranda; participants' diaries and/or evaluation checklists; pharmacy dispensing records; recorded data from automated instruments; copies of transcriptions certified after verification for accuracy and completeness; microfiche; photographic negatives; microfilm or magnetic media; x-rays; participant files; and records kept at the pharmacy, laboratories, and medico-technical departments involved in the study).

Source documents are commonly referred to as the documents—paper-based or electronic —upon which source data are first recorded. All study sites must comply with the standards of source documentation specified in the ICH E6 GCP and the **MATRIX GDP Policy** found on the MATRIX website (https://www.matrix4prevention.org/resources/matrix-policies).

As a condition for study activation, each study site must specify the source documents for all study procedures in the **Source Document SOP**. See SSP section 1.12 for study-specific source documentation types. A **Source Document SOP** template is available in the MATRIX-007 website. Supplemental information on the use of chart notes, visit checklists, and forms provided by the MATRIX CTH and/or MATRIX-007 CRMs is provided below.

1.8.1 Chart Notes

Study staff must document every contact with a study participant in a signed and dated chart note or contact log specifying the following information when necessary to document adherence to protocol requirements:

- Visit date at which a contact or procedures takes place
- Visit type (scheduled, interim, etc.)
- Purpose of the visit and location of the contact if other than the research clinic
- General status of the participant at the time of the visit

Chart notes also should be used to document the following, **as applicable:**

- The informed consent process (if an Informed Consent Coversheet is not used)
- Procedures performed that are not recorded on other source documents
- Additional information related to clinical exam findings to ensure appropriate follow-up
- Study-specific counseling and any associated referrals
- Types of medical records reviewed and other pertinent information in medical records not documented on other source documents
- Other pertinent data about the participant that are not recorded on other source documents and/or clarifications or information needed to supplement data recorded on a CRF
- Reason(s) why protocol-specified procedures were not performed
- Explanation of why procedures in addition to those listed on a checklist were performed
- Contact attempts to follow up on participants who missed a scheduled study visit or require other follow-up

A **Chart Note template** is available on the MATRIX-007 webpage under Study Documents (https://www.matrix4prevention.org/activity-hubs/clinical-trials/matrix-007-care-prep/matrix-007-care-prep-study-documents).

1.8.2 Visit Checklists

Visit checklists are convenient tools which may serve as source documentation if designed and completed appropriately. These checklists alone may not be sufficient for documenting all procedures but can be used to indicate that the procedure was completed. Chart notes may be required to supplement the information recorded within visit checklists. Visit Checklist templates are available on the MATRIX-007 webpage under Study Documents (https://www.matrix4prevention.org/activity-hubs/clinical-trials/matrix-007-care-prep/matrix-007-care-prep-study-documents).

Tips for completing visit checklists in accordance with these requirements are as follows:

- Enter the participant identification(s) (PID) number and visit date/code on the top section of each checklist. If checklists are multiple pages, enter the PID and visit date/code on each page.
  - For Enrollment visits, indicate the screening attempt in the applicable checklist item.
- Enter your initials only beside the procedures that you perform. Do not enter your initials beside procedures performed by other staff members.

- Ideally, only one person should initial each line of the checklist. If the line includes multiple procedures and they are performed by different staff, indicate who performed which procedure in the comments. Checklists should be designed to avoid this practice.
- If all procedures listed on a checklist are performed on the date entered in the top section of the form, the date need not be entered beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item.
- For items on the checklist that contain checkboxes, one set of initials is still sufficient, even if multiple boxes are checked.
- If a procedure listed on the checklist is not performed, enter "N/D" for "not done" or "N/A" for "not applicable" beside the item and record the reason why on the checklist (if not self-explanatory); initial and date this entry.

The sequence of procedures presented on the template visit checklists is a suggested ordering. In consultation with the MATRIX-007 CRM, site staff should modify the checklists to maximize the efficiency of site-specific study operations. Visit checklists and visit flow should be monitored and updated as needed to ensure that study visits are completed as quickly as possible, with minimal delays for participants and study staff.

1.8.3 Case Report Forms (CRFs)

The CRFs for this study are designed for use with the REDCap data management system (see SSP Section 6 Data Management for further details regarding the use of CRFs with REDCap). As specified in the Source Documentation SOP template, electronic CRFs are designed to be used as source, whenever possible. Prior to study activation, **each study site will document the CRFs to be used as source documents, CRFs that will not be used as source, and specify non-CRF source documents in the Source Documentation SOP.** The specifications must be followed consistently for all study participants. If study staff are not able to record data directly onto electronic forms designated as source documents, the following procedures should be undertaken:

- Record the data onto an alternative source document
- File the alternative source document into the participant's study chart
- Transcribe the data from the alternative source document onto the appropriate form and enter a note on the form stating the alternate source document used
- Write a chart note stating the relevant study visit date and the reason why an alternative source document was used
- Perform quality control procedures as specified in SOPs to ensure accurate and correct data transcription

1.9 Essential Documents

Study staff are responsible for the proper collection, management, storage, quality control, and quality assurance of all study-related documentation. This section contains information on the essential documents that each site must maintain throughout the study. Essential documents may be stored electronically and original (source) paper documents should be stored locally in a secure

location, depending on the document type. Although all required documentation must be available for inspection at any time, all documents need not be stored together in one location.

Teams are advised to save electronic versions of essential documents in the relevant MATRIX-007 section of the CARE PrEP Data SharePoint site, as applicable. Table 1-4 shows examples of essential documents specific to (but not limited to) MATRIX-007 and where/how they should be stored.

Table 1-4: Example Essential Document Storage

Document	Storage
Protocol, Guidance Documents, SOPs, and Plans	
MATRIX-007 protocol, Version 1.0 (and (CMs)s/ Protocol Amendments, as applicable)	Electronically accessible to all country team members & printed as needed for reference
MATRIX-007 SSP manual, Data Communiqués, data and operational guidance documents	Electronically accessible to all country team members& printed as needed for reference
MATRIX-007 partner/implementing partner policies and procedures (e.g., SOPs) relevant to study implementation	Electronically accessible to all country team members& printed as needed for reference
MATRIX-007 Study SOPs	Electronically accessible to all country team members & printed as needed for reference
Personnel Qualification Documents, Training Records, and Delegation Documents	
CVs, GCP and Human Subjects Protection (HSP) training certifications, IoR training documentation, 42 CRF 50 FDs, clinical licenses as applicable	Electronic, including on SharePoint
Completed PSPs, MATRIX IoR Forms, and DoD Logs	Electronic, including on SharePoint; scan and retain originals
Study staff team training documentation (e.g., agenda, materials, sign- in sheets)	Electronic, including on SharePoint; scan sign-in sheets, and retain originals
SSP manual and SOP Training logs	Electronic, including on SharePoint; scan sign-in sheets, and retain originals
All Regulatory Communications (IRB/IEC) and Contracts	
Submission packets	Electronic, including on SharePoint
Regulatory approvals (initial and subsequent reviews)	Electronic, including on SharePoint; scan and retain originals
Executed IRB/IEC authorization agreements (i.e., ceding documentation)	Electronic, including on SharePoint
Contracts (all), including between MATRIX country partners and implementing partners of study sites	Electronic, including on SharePoint; scan and retain originals
MATRIX-007 Communications	
All site responses to priority emails (thereby indicating they were read and responded to)	All responses should be retained in country PI and country study coordinator email (inbox/archive)
All management team and/or sponsor communications that document agreements or significant decisions involving study conduct, protocol deviations (PDs),	All communications should be retained in country PI and country study coordinator email (inbox/archive) or electronically filed

Document	Storage
eligibility and informed consent, safety and/or study endpoints, or study product	as relevant; the CRM will keep parallel records on SharePoint
Final study activation checklists	Electronic, including on SharePoint
Site operational visit documentation, including action item completion documentation	Electronic, including on SharePoint
Emails and other key communications from the LOG	All communications should be retained in country PI and Lead Study Coordinator email (inbox/archive) or electronically filed as relevant; LOG members will keep parallel documentation
Site field reports, site visit reports	Electronic, including on SharePoint
Study Source Documents/Data	
Informed Consent Forms and Informed Consent Coversheets	Original signed forms stored securely at study site or country team office
Data collection materials i.e., Case Report Forms (CRFs), including documentation of participant meeting study eligibility criteria	Within the study database; any original (source) paper versions should be retained securely at study sites
Test results/logs (all specimen data, including repeat or reanalysis performed for a test sample)	Paper-based source data stored securely onsite
Chart notes	Stored securely onsite within participant binders
Data obtained from non-study sources (e.g. non-study medical records) if required per SSP to be filed	Sources documented in chart notes; Certified copies of any paper-based medical records/testing results
Participant Tracker	Stored electronically (participant visit and contact attempt log) on secure site/country team systems and/or paper-based (daily activity log)
Participant locator information	Paper-based stored securely on-site
Protocol deviation/violation reporting documentation	Within the study database; paper-based submission to IRBs stored securely at study site or country team office
Safety sub-committee query responses	Electronic, including on SharePoint
Other Study Materials (Country/Site-specific Versions)	
Factsheets, study recruitment materials, and other study informational/educational materials	Electronically accessible to all country/site team members; printed as needed for use
Counseling materials, job aids, other tools	Electronically accessible to all country/site team members; printed as needed for use

When developing an essential documents filing structure for MATRIX-007, study sites are encouraged to consider their experiences implementing previous study protocols. While taking into account these experiences, the structure should be tailored to meet the specific needs of MATRIX-007, and ensure that all required documents are properly filed. The following are considerations and suggestions relevant to essential document filing:

- The MOSAIC/MATRIX-007 SharePoint site should be the primary electronic storage location for non-confidential essential documents.
- Teams may choose to have the protocol, SSP manual, SOPs, and other operational guidance documents accessible on an electronic platform or printed for easy access by country team members, especially site team members and implementing partner staff. All local or printed documents should be updated if/when new versions are released, and the older versions should be archived.
- It is recommended that MATRIX-007 confidential participant information be stored separately from other essential study documents.

Note: When essential documents are modified or updated, the original version and all modified or updated versions must be retained.

1.10 Good Documentation Practices (GDP) Policy

Study records documenting clinical (biomedical and/or behavioral) research study development, management, communication, conduct, analysis, and reporting must be created and maintained by each group and investigator of the CATALYST study according to the MATRIX GDP policy (available at https://www.matrix4prevention.org/resources/matrix-policies). This policy sets minimum standards for GDP compliance. The GDP policy also applies to guidance documents and plans issued by the study management team.

1.11 Protocol Deviations

Any change, divergence, or departure from the procedures defined in the IRB/IEC-approved study protocol is considered a protocol deviation (PD). Noncompliance may be on the part of the participant, the investigator, the study staff, or a combination of these groups. Efforts should be made to avoid PDs and correct any related issues that are identified. In MATRIX-007, a subset of PDs may be defined as **reportable** and require a formal corrective and preventative action plan (CAPA). See the MATRIX-007 CRF Completion Guidelines for a listing of reportable deviations. Additionally, any PD outside of this list that requires reporting to local IRBs/IECs, per institutional policies, should be reported on the CRF as 'other'.

If there is any question about whether a PD meets the definition of "reportable," sites may consult the Leadership and Operations Group (LOG) prior to making a formal report.

All reportable PDs must be entered into REDCap and reported to the LOG within **seven** days of site awareness. Procedures for reporting a PD:

- Complete the **Protocol Deviation CRF** under the participant record in REDCap that was impacted by the deviation. If a PD impacted more than one participant, complete a PD CRF under each impacted participant record.
- Notify the LOG that a new PD report is available. The email notification should contain the following:
  - **TO:** MATRIX007LOG@lists.matrix4prevention.org
  - **CC:** Copy the country PI and SC for their simultaneous awareness of the event
  - **Subject**: Protocol Deviation Report – (Country, Site)
  - **Email Narrative** (copy and paste the below listing into the body of the email to help ensure that all the required information is included):

This email is to notify you of a new/updated protocol deviation posted to the SharePoint site:

- **Date of Site Awareness:**
- **PID(s) or N/A:**
- **Country:**
- **Site name:**

Note: DO not attach a copy of the PD in the email.

PDs will be reviewed by the LOG through REDCap as part of ongoing study implementation oversight and quality monitoring. The MATRIX-007 CRM will be responsible for reviewing PD reports in real time and following up with the relevant country team for more information, as needed. On a routine basis, CRM will reconcile received reports with country teams to confirm all PDs have been reported to the LOG and that PDs have been submitted to IRBs/IECs as specified by IRB/IEC policy. The LOG may involve other management team members in the review of PDs depending on the issue being reported.

The LOG will respond to the PD submission within seven days and confirm that the proposed CAPA is adequate or provide comments/suggestions to strengthen the proposed CAPA. Country PIs are responsible for submitting PD reports to local IRBs/IECs as needed and within the required timelines, based on local policies.

1.12 Participant Confidentiality, Document Organization, and Retention

1.12.1 Participant Confidentiality

All documents containing participant information must bear a participant identifier, which generally will consist of either the PID or the participant's name. The PID should be used whenever possible to maximize participant confidentiality. All study databases must be secured with password-protected access systems. Any documents that link PIDs to other participant identifiers should be stored securely (locked in a cabinet/drawer if hard copy; password-protected if electronic) and it is recommended that these materials be stored in a location separate from individual participant records (i.e., those that identify participants by either PID or name). When in use, documents that link PIDs to other participant identifiers should not be left unattended or otherwise accessible to study participants, other study clinic clients, or any other unauthorized persons. Any documents transferred or transmitted to a non-study site location must be identified by PID only. Country teams may arrange to store completed ICFs at the MATRIX-007 country partner office; the same guidance applies to securing such documents. Care should also be taken to only refer to participants by PID in email communications.

Regardless of whether the identifier on a document is the participant name or PID, the original identifier may not be obliterated or altered in any way, even if another identifier is added. When necessary to maintain confidentiality, identifiers may be obliterated on copies of original source documents. For example, if medical records obtained from a non-study health care provider bear the participant's name, the original documents bearing the name must be stored unaltered with other study documents bearing the name. However, a copy of the original documents could be made, the PID could be entered onto the copies, and then the participant name could be

obliterated from the copies. Copies handled in this way could then be stored in participants' study files.

1.12.2 Document Organization

Study staff must make every effort to store all study records securely and confidentially. Study staff are responsible for purchasing file folders, binders, storage cabinets, and any other equipment or supplies needed to properly store all records.

Paper-based documents containing participant information and data must be stored in secure, lockable spaces (such as a filing cabinets), with limited access to only authorized study staff. Each enrolled participant should have a file containing any document baring their name (Name File) and a separate Participant Chart containing all documents identifiable by PID only. Participant charts are best organized using a 3-rings binder with file organizer sheets, where documents can be easily added or organized in sections. The **MATRIX-007 Name Linkage Log** is the sole document (paper-based) that links the participant's name to their PID for each study site. This log must be stored in a manner that no unauthorized person can obtain the name file and link it to the PID files or vice versa. Suggested storage option is to keep the name files and participant charts locked in separate files and the Name Linkage Log kept with the name files. Teams should consider an organized system where name files can be easily retrievable for each study visits. These documents can be stored together in one file, ideally in the same location as other name-based documents. Table 1-5 below is an example what types of source documents should be stored in the name file and the participant chart. See SSP Section XX for guidance on taking and storing photos of medical records.

Table 1-5: Participant Source Document Filing

Filed by Name	Filed by PID
Name Files by Participant • Informed Consent • IC coversheet • Participant Locator Form • Health Care Provider Form • Pre-screening Form • Permission to Contact Form (from CATALYST), if applicable • Any other document identifiable by name only (NO PID present)	**Participant Chart by Participant** • Visit Checklists • Chart notes • Completed paper-based Ultrasound Results CRF • Other completed paper-based CRFs • Certified copies of medical records and test results (No name present) • Printed GA dating Tool
Screening File by site (for those in-progress or not enrolled) • Pre-screening forms • IC coversheets • Informed Consents • Participant Locator form	**POC Testing Logs by site** • Pregnancy • HIV Testing • Syphilis

1.12.3 Document Retention

All essential source documents must be retained throughout the duration of the study and for at least three years following the end of data collection for MATRIX-007 (i.e., the date of final data

collection across all sites). Study records should not be re-located to an off-site location or destroyed without prior approval from the MATRIX Prime/CTH as detailed in the MATRIX GDP Policy (available at https://www.matrix4prevention.org/resources/matrix-policies). Country teams should abide by local IRB/IEC policies for retention and storage if they are more stringent than those outlined in this SSP manual. See more guidance in SSP section 6 Data Collection and Management.