MATRIX-001 Study-Specific Procedures (SSP) Manual
Section 1 – Introduction

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1 Introduction

This section specifies the sources of procedural information available to study staff, the responsibilities of Investigators of Record (IoR), and the process by which each site will be approved to initiate implementation of MATRIX-001.

1.1 Current Protocol Specifications

Table 1 below documents the history of the MATRIX-001 protocol, along with any Clarification Memos (CM) and Full Amendments, if applicable, all of which are considered Essential Documents. A copy of each document should be available to staff and a copy should be maintained in site essential files. It is not necessary for sites to file copies of the below-mentioned documents in the SSP Manual itself.

Table 1: MATRIX-001 Protocol History

Document	Date
MATRIX-001 Protocol, Version 1.0	04 MAY 2023
CM #1	22 AUGUST 2023
CM #2	27 SEPTEMBER 2023

Sites are expected to operate under the protocol version that is currently approved by the local institutional review board/independent ethics committee (IRB/IEC), other applicable regulatory bodies and associated CMs. To ensure this section reflects the current specifications of the protocol, upon issuance of any future protocol Clarification Memo (CM) or Protocol Amendment, specifications listed above will be updated accordingly.

These documents are available on the MATRIX-001 webpage (https://www.matrix4prevention.org/activity-hubs/clinical-trials/matrix-001).

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-001 Management Team about this and document contingency plans related to COVID-19 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.

1.2 Sources of Procedural Information

The Study Specific Procedures (SSP) Manual serves to supplement the 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 specifications in the protocol will take precedence. In the event study implementation questions are not adequately addressed by the study protocol or this manual or if any inconsistencies between the two documents are identified, please notify the MATRIX-001 Study Management Team at [matrix001mgmtteam@lists.matrix4prevention.org].The Management Team should also be consulted for general questions on protocol implementation or study procedures, including clinical, lab, product, behavioral assessments, and/or data or case report form (CRF) completion procedures.

This group consists of the Protocol Chair(s) and representatives from the study sites, MATRIX Prime/Clinical Trials Hub (CTH), Design to Delivery (D2D) Hub Pillar 2, USAID, and CONRAD.

1.3 Investigator Responsibilities

MATRIX-001 must be conducted in accordance with the relevant United States (US) Code of Federal Regulations (CFR) and the International Conference on Harmonization Consolidated Guidance for Good Clinical Practice (GCP). MATRIX-001 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.

Each site IoR must sign an Investigator Signature Form (protocol signature page; PSP) and a U.S. Food and Drug Administration (FDA) Form 1572 if IND study to formally indicate his/her agreement to conduct MATRIX-001 in accordance with the study protocol, applicable US regulations and MATRIX policies. A copy of the PSP can be found in the MATRIX-001 protocol. A PSP must be signed by the IoR and sent to the MATRIX Prime/CTH Regulatory (matrixregulatory@lists.matrix4prevention.org) and CONRAD for all initial protocol versions and full protocol amendments. The site will keep copies of the PSP and 1572(s) on site with their essential documents. The obligations and responsibilities assumed by the IoR when signing the FDA Form 1572 and PSP are listed on the forms themselves. Updates to the 1572 should be submitted to the MATRIX Prime/CTH Regulatory (matrixregulatory@lists.matrix4prevention.org) and CONRAD, with a short summary of any updates that were made. If there is a change in IoR/PI, a revised 1572 and a new PSP should be submitted to the MATRIX Prime/CTH and CONRAD. Additionally, sites should notify the MATRIX Prime/CTH and CONRAD of the change in IoR/PI and complete any other documentation requested.

The IoR may delegate his/her obligations and responsibilities for conducting MATRIX-001 to other qualified study staff members; however, delegation does not relieve the IoR of his/her ultimate responsibility for all study procedures performed and all study data collected. Delegation of IoR responsibilities must be formally documented on the site's Delegation of Duties (DoD) Log throughout study implementation.

Note: No staff member should fulfill the IoR role in the IoR's absence. Full responsibility and authority over the protocol by anyone other than the IoR/PI may only take place if an additional 1572 is completed and submitted to the MATRIX Prime/CTH Regulatory (matrixregulatory@lists.matrix4prevention.org) and CONRAD. This new IoR will be required to sign the PSP in the current version of the MATRIX-001 protocol and to update the site's DoD Log.

Staff regularly involved in the source documentation of safety data or are delegated to perform critical trial related procedures should be included on the 1572 as a sub-investigator. Such components may include, but are not limited to, adverse event (AE) assessment, provision of informed consent, collection of participant safety information, confirmation of participant eligibility, or dispensation of study product.

Consistent with the regulations, guidelines, and policies cited above, the site IoR must obtain and maintain IRB/IEC (and if applicable, drug regulatory authority [DRA]) approval of MATRIX-001 throughout the period of study implementation. All sites are strongly encouraged to request an acknowledgement of receipt for all documents submitted to their IRBs/IECs/DRAs and to request that IRBs/IECs/DRAs note the effective and expiry dates of all approvals. Documentation of all correspondence to and from all responsible IRBs/IECs/DRAs (i.e., complete copies of all submissions, responses, and approvals) must be maintained in on-site essential document files. Documentation of all IRB/IEC/DRA approvals may also be requested by the MATRIX Prime/CTH and CONRAD.

1.4 Study Activation Process

Prior to undertaking any study procedures, the study site must obtain approval to conduct MATRIX-001 from all required regulatory authorities and IRBs/IECs. The site also must complete study activation procedures with the Study Management Team and CONRAD.

The MATRIX Prime/Clinical Trials Hub (CTH) will issue a Site-Specific Study Activation Notice to each site when all study activation requirements have been met. No protocol-specified study procedures may be undertaken at a site prior to issuance of the Site-Specific Study Activation Notice.