



# MATRIX-001 Study-Specific Procedures (SSP) Manual

## Section 12 – Data Collection

### TABLE OF CONTENTS

12	Introduction .....	1
12.1	OpenClinica Overview .....	2
12.1.1	Data Entry/Quality Control .....	3
12.1.2	Electronic Signatures by Investigators .....	3
12.2	Case Report Forms (CRF) .....	4
12.3	CRF Completion.....	4
12.3.1	General Guidelines.....	4
12.3.2	Screening and Enrollment/Randomization.....	4
12.3.3	Replacement Participants .....	5
12.3.4	Site Data Management SOP .....	5
12.4	Study-Specific Data Collection Information .....	5
12.4.1	Participant Identification Numbers (PTID).....	5
12.4.2	Study Visit Timing.....	6
12.4.3	Visit Folders and Visit Codes .....	8
12.4.4	Form Supply.....	9
12.4.5	CRF Completion Schedule.....	9
12.4.6	Completing Interviewer-Administered Forms.....	10
12.4.7	Site Review (Quality Control) of CRFs.....	10
12.5	Form-Specific Completion Instructions.....	11
 <b>Table 1:</b> MATRIX-001 Statistical and Data Management Staff .....		 2
<b>Table 2:</b> MATRIX-001 Visit Code Assignments for Required Follow-up Visits .....		8
<b>Table 3:</b> MATRIX-001 Schedule of Forms – CRFs Required to be Completed at Each Visit.....		9

## 12 Introduction

The purpose of this document is to provide site staff with the information they need to successfully complete and submit MATRIX-001 Case Report Forms (CRFs). For questions about this section or about general data collection policies, procedures, or materials, please contact the FHI 360 Clinical Data Manager for the study as listed below.

The SDMC (Statistical and Data Management Center) for this study is FHI 360. FHI is located in North Carolina, USA, and is in the US Eastern Time (ET) time zone. The FHI 360 team members, along with their job role and e-mail address, are listed below.

**Table 1:** MATRIX-001 Statistical and Data Management Staff

Job Role	Name	Email Address
Protocol Statistician(s)	Rachael Fuchs (lead) Irena Brates (support)	<a href="mailto:RFuchs@FHI360.org">RFuchs@FHI360.org</a> ; <a href="mailto:IBrates@fhi360.org">IBrates@fhi360.org</a>
Clinical Data Manager(s)	Michele Fanton (lead) Anne Heath (backup)	<a href="mailto:MFanton@FHI360.org">MFanton@FHI360.org</a> ; <a href="mailto:AHeath@FHI360.org">AHeath@FHI360.org</a>
Clinical Programmer(s)	Phillip Cardella Amy Fiori	<a href="mailto:PCardella@FHI360.org">PCardella@FHI360.org</a> ; <a href="mailto:AFiori@FHI360.org">AFiori@FHI360.org</a>

## 12.1 OpenClinica Overview

OpenClinica is the data management system used by FHI 360 to receive and manage study data collected at study sites. Each site completes study electronic case report forms (eCRFs) by entering data into the OpenClinica study database. As specified in each site’s Source Documentation SOP, data may be entered directly into the study database (i.e. eCRF is source), collected first on paper CRFs and then entered into the study database, and/or entered into the study database based on other non-CRF source documents (e.g., lab reports, testing logs, chart notes, etc.)

The MATRIX-001 study database in OpenClinica may be accessed at <https://fhi360.openclinica.io/>

When using OpenClinica, the internet browser chosen and connectivity quality will be the most critical factors affecting functionality, as OpenClinica is accessed via a URL using a web browser.

Users using outdated browsers will see a new warning banner on the log-in page of

OpenClinica. This warning will inform them that their browser does not support security features that are being implemented in future OpenClinica releases and to upgrade their browser. Users will see this warning banner if they use any of the following browsers:

- Internet Explorer - Versions older than 8.0
- Chrome - Versions older than 30.0
- Firefox - Versions older than 24.0
- Safari - Versions older than 7.0
- Opera - Versions older than 17.0.

Each site’s Data Management SOP designates the site staff members responsible for entering data into the study database. FHI 360 grants designated site staff access with specific user permissions to the study database. They are required to complete eLearning modules in OpenClinica, as assigned by FHI 360, before access is granted and data can be entered into the study database. For more detailed information, see the OpenClinica Guide, posted on the MATRIX-001 webpage under Study Documents.

Detailed guidance on data collection, entry, navigation and general use of OpenClinica is provided in the OpenClinica Electronic Data Capture (EDC) Training Manual, which is posted on the MATRIX-001 webpage under Study Documents.

Site staff should contact the study Clinical Data Manager with any questions related to study data collection and management. Technical questions or problems related to access or use of the OpenClinica software should be directed to the Data Management team member. If OpenClinica support is needed, the Data Management group will liaise with the EDC support for further assistance and troubleshooting.

### 12.1.1 Data Entry/Quality Control

Once an eCRF is completed and saved in the study database, the following may occur:

- A system query may be automatically triggered in OpenClinica (e.g., denoting incomplete or inconsistent data).
- Review may be required for certain forms and/or fields by the FHI 360 Clinical Data Manager, and manual data queries may be placed.
- Review may be required for certain forms and/or fields by the site monitor (i.e., PPD), and data queries may be placed.
- MedDRA coding will be required for AE Log CRFs, and coding queries may be placed.
- AE-EAE reconciliation will occur and inconsistency queries may be placed.
- WHO coding will be required for CM Log CRFs, and coding queries may be placed.

Queries are listed in the OpenClinica Task Summary on the study home page of designated site users. Designated site staff members are responsible for routinely checking the Task Summary and correcting/updating study data to resolve any outstanding queries.

When site staff correct/update study data and/or enter a query response to address a manual or coding query, FHI 360 staff review the updated data and/or response, and resolve the query or re-query as needed.

When site staff correct/update study data and/or enter a query response to address a monitoring query, the site monitor (i.e., PPD) reviews the updated data and/or response, and resolves the query or re-queries as needed.

If a site utilizes paper CRFs as source documents, any changes to the paper CRFs **must** be entered into the OpenClinica study database.

### 12.1.2 Electronic Signatures by Investigators

Each site investigator or designee is expected to complete a single sign-off of a participant's study data (one sign-off for each participant at his/her site) once the participant terminates from the study and site staff have resolved all data queries for the given participant. By completing this participant-level sign-off in the OpenClinica study database, the investigator or designee attests that the data has been reviewed and is deemed to be accurate. OpenClinica users will use their login credentials as their electronic signature (see image below). Please refer to the "Electronic Signature" section of the OpenClinica Electronic Data Capture (EDC) Training Manual and/or the Investigator e-Learning module for specific instructions.

## 12.2 Case Report Forms (CRF)

The current version of the MATRIX-001 case report forms can be found at the MATRIX-001 web page under Study Documents.

## 12.3 CRF Completion

Please refer to the OpenClinica guidelines posted on the MATRIX-001 web page under Study Documents.

### 12.3.1 General Guidelines

To the extent possible, site staff should utilize direct data entry into the OpenClinica study database so that the eCRF serves as the source document. Direct data entry is especially encouraged for data collection based on participant self-report.

When direct data entry is not possible due to the nature of the source data - for example, when the source data is a local lab results report - site staff are encouraged to enter study data into the OpenClinica study database based on the site-specific source document (in this case, the local lab results report).

- Site staff are encouraged to avoid paper CRF completion, as it represents an additional, intermediate step of data management and QA/QC review into site data management workflows. In addition, paper CRF completion introduces the risk of data transcription errors, and could contribute to database data entry errors.

When completing an eCRF, refer to the CRF Completion Guidelines (CCG) document, for detailed instructions on data collection pertaining to the given form and fields on that form.

Complete eCRFs as soon as possible once the data is available and has undergone internal QC review, as applicable. Ideally, completion of all required eCRFs for a given visit will occur within 1–2 business days of the visit, though up to 7 days is acceptable.

### 12.3.2 Screening and Enrollment/Randomization

Data entry into the study database begins at the Screening Visit. Once a participant is determined to be eligible, enrolls, or fails a screening attempt, study eligibility data should be entered into the study database as follows:

- For participants who screen but do not enroll in MATRIX-001, data entry is required for the Inclusion Exclusion Criteria eCRF (located in the Enrollment folder). (Some eCRFs that were completed during the failed screening attempt may remain in the study database, but may not undergo QC review).
- For participants who enroll in MATRIX-001, enter data for the Inclusion Exclusion Criteria eCRF, along with all required Enrollment Visit CRFs.

**Randomization:** The first step in the randomization process is for site staff to complete the Inclusion Exclusion Criteria CRF. To randomize a study participant, site staff must complete the Randomization Input

CRF and save the page. The Randomization Output form will display the assignment. Refer to the CCG for specific instructions on how to complete the Randomization CRF.

### **12.3.3 Replacement Participants**

If it has been determined by the Management Team that a participant needs to be replaced, a replacement subject will be enrolled into the study as detailed above and in the CCG.

### **12.3.4 Site Data Management SOP**

As a condition for study activation, each study site must have a site or study-specific SOP for Data Management. This SOP should be reviewed and followed in combination with the information contained in the study protocol, this SSP Manual, and the site's Clinical Quality Management Plan (CQMP).

The Data Management SOP outlines site staff responsibilities and contains information on several data topics, including:

- Participant ID (PTID) assignment
- Participant study file organization
- Participant confidentiality
- Site data quality control (QC) processes
- Timing of data entry into the study database
- Data storage
- Data security
- Contingency plans in case of interrupted access to the study database.
- Management of site user account permissions for access to the study database.

## **12.4 Study-Specific Data Collection Information**

Please refer to the CRF Completion Guidelines (CCG) for details about data collection in EDC.

### **12.4.1 Participant Identification Numbers (PTID)**

As described in each site's Data Management SOP, each participant that provides written informed consent to be screened in MATRIX-001 will be assigned a MATRIX-001 PTID. To do this, site staff will generate in OpenClinica a participant number (called "Subject ID" in OpenClinica) within the electronic study and site folder; this number will serve as the participant's PTID. Refer to the "Creating Subjects" section of the OpenClinica Electronic Data Capture (EDC) Training Manual and the CCG for specific instructions.

Each PTID is unique. It will be assigned to a single participant only at a given site, and not assigned to any other participant at any site or in any study (e.g., MATRIX) for which FHI 360 is the Statistical and Data Management Center (SDMC).

Each site will be provided with a PTID-Name Linkage Log and site staff will maintain this document, which will be used to link a participant’s name with their assigned PTID. For study purposes, the act of MATRIX-001 PTID assignment is defined as completion of an entry on the MATRIX-001 PTID-Name Linkage Log for a given participant.

The MATRIX-001 PTIDs are 8 digits and formatted as “XXXXYYYY”. The PTID consists of two parts: the site number (XXXX) and the participant number (YYYY). The PTID will continue sequentially at each site.

SITE	PTID FORMAT
CAPRISA	SA01-1001
EVMS	US01-1001
KEMRI	KE01-1001

### 12.4.2 Study Visit Timing

Please refer to SSP 5 – Study Procedures for visit windows.

#### 12.4.2.1 Screening and Enrollment

The initial screening visit is defined as the day the participant provided written informed consent to be screened for the study. The Enrollment Visit will be scheduled to take place within 8 weeks of the initial Screening Visit. The date the participant is enrolled/randomized is Study Day 0 for the participant. A visit window calendar tool in Microsoft Excel that can be used to calculate the allowable window for study enrollment based on the participant’s screening date (i.e., date informed consent provided for the current screening attempt).

#### 12.4.2.2 Screening Attempts (Re-Screens)

If a participant’s first screening attempt is unsuccessful, she may re-screen once if she chooses. If she does re-screen, all screening procedures must be repeated with the exception of PTID assignment. Once a PTID is assigned to a participant that PTID is used for the re-screening procedures and forms completed for that participant (do not assign a new PTID).

If a participant re-screens and enrolls, all previously completed eCRFs (from the original, failed screening attempt) must be updated to reflect only data from the successful Screening and Enrollment Visit. Note however, the Inclusion Exclusion Criteria eCRF completed during the failed screening attempt should be updated to reflect the participant’s final eligibility status and enrollment into the study.

#### 12.4.2.3 Follow-up Visits

For each MATRIX-001 follow-up visit, the visit type, visit code, target visit day, and visit window are listed in SSP 5. Target days and windows are listed in days, with the day of enrollment/randomization as study Day 0.

Note that scheduled visits cannot occur on weekends, which means the day of the week must also be taken into account when scheduling the Dose Administration Visits and PK/PD sampling visits (Visits 3-7).

#### **12.4.2.4 Target Days and Visit Windows**

Whenever possible, visits should be completed on the target day. If it is not possible to complete the visit on the target day, the visit should be completed within the visit window. Note that only certain visits have a window; many visits must be completed on the day specified in the visit window calendar tool.

FHI 360 will provide sites with a spreadsheet tool that may be used to generate individual participant follow-up visit calendars. The spreadsheet requires that the participant's Enrollment (i.e., randomization) date be entered. Once the enrollment date is entered, the target day and visit window for each required follow-up visit up through Visit 8 will appear.

#### **12.4.2.5 Missed Visits**

In those cases where a participant is not able to complete any part of a required follow-up visit within the visit window, the visit is considered "missed". The missed visit is documented on the Visit Summary Form.

#### **12.4.2.6 Interim Visits**

An interim visit (unscheduled visit) is a contact with a study participant that meets one of the following criteria:

- Additional study procedures and/or data collection are conducted outside of what is specified in the protocol for a required study visit. For example, an interim visit may occur via a phone contact if the participant reports a new AE. Required follow-up visit procedures are not done, either because the required follow-up visit has already been completed, the participant is in between visit windows, or it is too early in the visit window to complete the required visit.
- Required study visit procedures are conducted outside the visit window, either to make up certain procedures from a missed visit, or to conduct Visit 8/SEV/Early Termination Visit procedures due to an early product discontinuation (for reasons other than HIV infection or pregnancy). For example, if a participant permanently discontinues study product use at Visit 5, she would complete Visit 8 visit procedures at Visit 5, if able and willing.

All interim visits/contacts with the participant should be documented in a chart note. Additionally, if the interim contact results in at least one newly-completed eCRF, the interim visit is assigned an interim visit code (visit number ending in something other than ".0"). All phone contacts that meet interim visit criteria as specified above are also assigned interim visit codes. See section 12.3.2 for information on how to assign visit codes to interim visits.

For MATRIX-001, an Interim Visit Summary CRF is completed for interim visits/contacts as needed.

### 12.4.3 Visit Folders and Visit Codes

The eCRFs in the study database are set up within pre-defined study visit folders, so the visit name and visit code automatically appear (and do not need to be entered for required study visits). All log forms (i.e., AE Y/N and Log, Concomitant Medications Y/N and Log, Protocol Deviations Y/N and Log, Medical History Y/N and Log, and Product Hold Summary and Log) are housed in the "Ongoing Logs" folder within the study database. The Discontinuation of Study Product eCRF and Study Termination eCRF are housed within the "Discontinuations" folder; each of these forms is completed once for each participant to document his/her permanent product discontinuation and study exit, respectively. Pharmacy Dispensation is housed within its own Pharmacy folder. In addition, the Pregnancy Report, Pregnancy History, and Pregnancy Outcome eCRFs are housed within the Pregnancy folder (if applicable). Table 12-2 below lists the visit codes assigned to each required follow-up visit.

**Table 2:** MATRIX-001 Visit Code Assignments for Required Follow-up Visits

Visit	Visit Code
Screening	V1
Enrollment	V2
Randomization	V3
Post daily doses	V4
Start of alternate day dosing	V5
Post 5 <sup>th</sup> dose	V6
Post last dose	V7
Study Exit Visit	V8
Common Visits (log style forms)	N/A
Unscheduled Visit	UV

#### 12.4.3.1 Visit Codes for Split Visits

See Section 12.3.2 for a definition of split visits. When split visits occur, the CRFs completed for the visit are all assigned the same visit code, even though the dates will differ between some of the CRFs. For example, a participant comes in on her Visit 4 target day of 23-AUG-23 and completes all required visit evaluations except pregnancy testing. She returns on 24-AUG-23 (still within the visit window) and provides a urine sample for pregnancy testing. All CRFs dated 23-AUG-23 and 24-AUG-23 are assigned the same visit code of "V4" and are housed within the Post Daily Doses visit folder in the study database.

#### 12.4.3.2 Visit Codes for Interim Visits

Note that interim visit (unscheduled) codes are not used for visits/contacts between the Screening Visit and Enrollment Visit, as these contacts are considered part of the screening process.

Unscheduled visits will be numbered automatically in OpenClinica as they are added for the participant.



#### 12.4.4 Form Supply

FHI 360 will post a CRF (pdf) file, representing output from the study database eCRFs, on the MATRIX-001 webpage under Study Documents.

The pdf file represents the complete set of study CRFs and may be used by site staff for local IRB submission as needed, as well as for printing their own paper CRF supplies as back-up in the case completing eCRFs in OpenClinica is not possible.

#### 12.4.5 CRF Completion Schedule

The FHI 360-provided forms for this study include all forms that are completed and entered into the study database.

Some FHI 360-provided forms are required to be completed at each visit, while other forms are required only at one visit or only when specifically indicated. The following table (Table 12-3) lists the forms that are required to be completed at each study visit, as well as the forms that are completed on an “as needed” basis.

**Table 3:** MATRIX-001 Schedule of Forms – CRFs Required to be Completed at Each Visit

Visit	Form Name
<b>V1 – Screening</b>	Demographics, Eligibility Form, Informed Consent, Basic Medical and Menstrual History, Point of Care Form, Pelvic Exam Form, Visit Summary Form, Vital Signs and Physical Exam, Screening Lab, Genital Swab Results, Lab Results
<b>V2 – Enrollment</b>	Visit Summary Form, Basic Medical and Menstrual History, Point of Care Form, Pelvic Exam Form, Vital Signs and Physical Exam, Specimen Storage Form, Baseline Behavioral, Baseline Acceptability
<b>V3 - Randomization</b>	Randomization Input, Randomization Output, Clinical Observations, Point of Care Form, Initial Product Use Assessment
<b>V4</b>	Visit Summary Form, Dose Accountability Form, Basic Medical and Menstrual History, Point of Care Form, Pelvic Exam Form, Vital Signs and Physical Exam, Specimen Storage Form, Product Use Assessment (FU2)
<b>V5</b>	Visit Summary Form, Dose, Basic Medical and Menstrual History, Point of Care Form, Pelvic Exam Form, Vital Signs and Physical Exam, Specimen Storage Form, Clinical Observations
<b>V6</b>	Visit Summary Form, Dose, Basic Medical and Menstrual History, Point of Care Form, Pelvic Exam Form, Vital Signs and Physical Exam, Specimen Storage Form, Clinical Observations

Visit	Form Name
V7	Visit Summary Form, Dose, Dose Accountability Form, Basic Medical and Menstrual History, Point of Care Form, Pelvic Exam Form, Vital Signs and Physical Exam, Specimen Storage Form, Genital Swab Results Form, Product Use Assessment (FU3)
SEV/Early Termination	Study Stop Form/Final Disposition Form
As needed (Additional study procedures/Interim Visit procedures)	Unscheduled Visit Form
As needed (Ongoing Logs)	Product Interruption Form, Adverse Event Form, Concomitant Medications, Pre-existing Medical Conditions, Social Harm, Pregnancy Report, Pregnancy Outcome
Discontinuations	Study Stop Form/Final Disposition Form

#### 12.4.6 Completing Interviewer-Administered Forms

In order to standardize interviewer-administered data collection from site to site and to maximize quality, it is critical that participant interviews be conducted with a non-biased, non-judgmental approach. Study staff should help a participant feel comfortable sharing personal information and opinions while asking the study questions in a consistent manner from participant to participant.

Site staff are encouraged to practice direct data entry when administering the interviewer-administered forms (i.e. Demographics), to the extent possible, so that the eCRFs serve as the source documents. Skip patterns are documented in the CRF Completion Guidelines (CCG) document, which site staff should reference when administering the forms. The CCG will be posted on the MATRIX web site along with the complete set of study CRFs (pdf file – see above section 12.3.4). The skip patterns are also programmed into the data checks within the study database, and system queries will be generated in real-time, as data is saved within the database, if required items are missed and/or inconsistent responses are entered. This real-time feedback will allow the interviewer to clarify participant responses and update/correct participant self-reported data during the participant interview, yielding accurate, consistent, and complete study data. Site staff who will conduct the participant interviews and complete the interviewer-administered behavioral and product adherence forms are encouraged to practice conducting the interviews, completing/updating the eCRFs by entering test data, and familiarizing themselves with the eCRF questions, skip patterns, and system queries prior to conducting actual participant interviews.

#### 12.4.7 Site Review (Quality Control) of CRFs

As described in the site's Data Management SOP [and referenced in the site's Clinical Quality Management Plan, (CQMP)], each site must perform Quality Control (QC) review steps, especially for paper CRFs (if used) prior to their data entry into the study database. While paper CRFs are being reviewed, it is important that they are stored and tracked systematically.

Below are specific review guidelines that should be followed for these QC review steps.

#### **12.4.7.1      MATRIX-001 QC Review Step #1 (completed during visit)**

- Review visit checklist and genital exam checklist (if used) to ensure all required procedures were completed
- Review eligibility checklists/worksheets to ensure completeness and verify participant eligibility
- Review LDMS Specimen Tracking Sheets to ensure completeness and accuracy
- Review completed CRFs based on participant responses to ensure completeness (see table 3 for list of CRFs per visit):

#### **12.4.7.2      MATRIX-001 QC Review Step #2 (completed after visit)**

- Review visit checklist to ensure all required procedures were completed
- Ensure the PTID is correct, is recorded correctly on all paper source documents (including paper CRFs, if used), and is the same on the paper source documents and the eCRFs for a given participant.
- Ensure that no participant identifiers other than the PTID are present on paper source documents, including paper CRFs (if used).
- Ensure that the assigned visit code is correct, and is consistent between the paper source documents, including paper CRFs (if used), the eCRFs, the LDMS Specimen Tracking Sheet, and LDMS for a given participant visit.

### **12.5 Form-Specific Completion Instructions**

Detailed form completion instructions for each form are provided in the CRF Completion Guidelines (CCG) document. The instructions document skip patterns and include guidance on completion of eCRFs in the study database. Some items on forms are straightforward and do not require specific instructions. Therefore, you will not see all form items listed in the CCG, but rather only those items needing detailed explanation.