**PURPOSE**

The purpose of this standard operating procedure (SOP) is to define source documentation requirements and procedures for MTN-043.

**SCOPE**

This SOP applies to all MTN-043 study staff at *[Insert site name]* that conduct study visits and/or complete source documents and case report forms.

**RESPONSIBILITIES**

MTN-043 staff members who complete study visits and/or complete MTN-043 study documentation are responsible for understanding and following this SOP.

MTN-043 *[Insert responsible staff]* is responsible for training study staff to collect and manage MTN-043 study data in accordance with this SOP, and for day-to-day oversight of staff involved in data collection and management.

MTN-043 QA/QC Manager is responsible for overseeing quality control (QC) and quality assurance (QA) procedures related to this SOP.

MTN-043 Site Leader/Investigator of Record has ultimate responsibility for ensuring that all applicable study staff follows this SOP.

PROCEDURES

Source documentation for MTN-043 will be completed in accordance with the DAIDS Standard Operating Procedure (SOP) for Source Documentation. This policy can be accessed at:<https://www.niaid.nih.gov/research/daids-clinical-site-implementation-operations>

*[Note to sites: if applicable, include here the text “Source documentation for MTN-043 also will be completed in accordance with the [list applicable national, local, or facility-specific documentation regulations and guidelines] (see Attachment x).”]*

Table A provided in Appendix 1 lists all the MTN-043 study procedures and associated source documents. Table B provided in Appendix 1 designates the MTN-043 Case Report Forms (CRFs) that will and will not be used as source documents. Part C lists the MTN-043 site-specific forms used as source documents.

Questions related to adherence to the DAIDS SOP for Source Documentation, the specifications of Appendix 1, and/or other aspects of this SOP will be directed to [*Insert responsible staff*]. Queries that cannot be resolved locally will be directed to MTN LOC (FHI 360) Clinical Research Managers and SCHARP Clinical Data Managers.

Definitions:

* Source data: All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies). [Source: ICH Consolidated Guidance for Good Clinical Practice (ICH-E6)]
* **Source documents:** Original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, participants’ diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies of transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the trial). [Source: ICH Consolidated Guidance for Good Clinical Practice (ICH-E6)]

Source documents are commonly referred to as the documents —paper-based or electronic — upon which source data are first recorded.

* **Certified copies:** See page 11 of the DAIDS SOP for Source Documentation

**ABBREVIATIONS AND ACRONYMS**

CRF Case Report Forms

DAIDS Division of AIDS

ICH International Conference on Harmonization

MTN Microbicide Trials Network

SCHARP Statistical Center for HIV/AIDS Research & Prevention

SOP Standard Operating Procedure

**APPENDICES**

Appendix 1 Part A, Listing of MTN-043 Procedures and Source Documents

Part B, MTN-043 CRFs and Source Documents

Part C, Site-Specific Forms Used as Source Documents

**REFERENCES**

ICH Consolidated Guidance for Good Clinical Practice (ICH-E6)

DAIDS SOP for Source Documentation (Version 2.0; 20 Dec 06)

FDA Guidance for Industry, Electronic Source Data in Clinical Investigations (Sep, 2013)

**REVISION HISTORY**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Version** | **Effective Date** | **Supersedes** | **Review Date** | Change |
|  | DD MMMYYY | N/A (initial version) | DD MMMYYY | Initial Release |

APPROVAL

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | |  |  |  |
|  | Author, Author’s Title | |  |  | Date: |
|  |  | |  |  |  |
|  | Approver’s Name, Approver’s Title | |  |  | Date: |
| **Appendix 1: Part A**  **MTN-043 Source Documentation of Study Procedures** | | | | | | |
| **Evaluation/Procedure** | | **Source Document(s)** | | | | |
| **ADMINISTRATIVE AND REGULATORY** | | | | | | |
| Obtain mother and infant informed consent | | Signed and Dated Informed Consent Forms  Informed Consent Coversheets (or chart note) | | | | |
| Assess informed consent comprehension | | Informed Consent Comprehension Assessment tool | | | | |
| Assign a unique Participant Identification (PTID) number | | MTN-043 PTID-Name Linkage Log | | | | |
| Assess and/or confirm eligibility | | Eligibility Checklist (signatures)Screening Behavioral Eligibility Worksheet  Enrollment Behavioral Eligibility Worksheet | | | | |
| Collect demographic and background information | | Demographics CRF, Infant Demgraphics CRF | | | | |
| Collect/review/update locator information | | Site locator documents (collect/update)  Visit checklist (review) | | | | |
| Medical records release and pediatric care provider information review | | Medical release form, Site-specific document, Signed Informed Consent Form | | | | |
| Randomization | | Randomization CRF | | | | |
| Provide reimbursement | | Visit checklist, site-specific reimbursement log, and/or chart note | | | | |
| Schedule next visit | | Visit checklist and/or chart note | | | | |
| BEHAVIORAL | | | | | | |
| Protocol counseling | | Chart note, Visit Checklist and/or site-specific document | | | | |
| Product adherence counseling | | Chart note, Product Use Adherence Counseling Worksheets, and/or site-specific document | | | | |
| Contraceptive counseling | | Chart note, Contraceptive Counseling Worksheets, and/or site-specific document | | | | |
| HIV/STI risk reduction counseling | | Chart note, HIV Pre/Post Test and HIV/STI Risk Reduction Counseling Worksheet, and/or site-specific document | | | | |
| HIV pre- and post-test counseling | | Chart note, HIV Pre/Post Test and HIV/STI Risk Reduction Counseling Worksheet, and/or site-specific document | | | | |
| PrEP Counseling | | Chart note, Visit Checklist and/or site-specific document | | | | |
| Behavioral Assessment | | Baseline Behavioral Assessment CRF  Behavioral Assessment – Follow Up CRF, and  Behavioral Assessment - Month 3 CRF | | | | |
| Product acceptability assessment | | Behavioral Assessment -Follow Up,  Behavioral Assessment - Month 3 CRF  Tablet Assessment  Ring Assessment | | | | |
| In-depth Interview (IDI) subset | | IDI completion documented on:  Qualtiative Visit Checklist, and IDI Checklists, IDI Tracking CRF  Qualitative Participant Log | | | | |
| Social Harms Assessement | | Social Impact, Social Impact Y/N and Social Impact Log CRFs | | | | |
| **CLINICAL** | | | | | | |
| Mother medical, pregnancy history | | Baseline Medical History Log CRF (all baseline conditions including clinical evaluations will be summarized here), chart notes  Pregnancy History CRF  Edinburgh Postnatal Depression Scale CRF | | | | |
| Infant feeding assessment | | Feeding Assessment - Screening and Enrollment CRF, Feeding Assessment Follow-up CRF, Feeding Inventory CRF, chart notes | | | | |
| Infant medical, pediatric care review | | Baseline Medical History Log CRF (all baseline conditions including clinical evaluations will be summarized here)  Pediatric care records  Chart notes | | | | |
| Record/update AEs | | Adverse Event Log CRF (infant and mother case books), Chart notes | | | | |
| Concomitant medications and vaginal products/practices | | Concomitant Medications Log CRF (infant and mother case books)  Vaginal Practices CRF  Visit Checklists | | | | |
| Physical examination (full or targeted) | | Vital Signs CRF  Physical Exam CRF (infant and mother case books)  Infant Vital Signs CRF  Infant Ages and Stages Questionnaire and CRF | | | | |
| Pelvic exam | | Pelvic Exam Diagrams  Pelvic Exam checklist | | | | |
| Disclose available test results | | Chart notes and/or visit checklist | | | | |
| Treat or prescribe treatment for UTIs/RTIs/STIs or refer for other findings | | Chart notes and/or prescription  Referral Letter | | | | |
| **LABORATORY** | | | | | | |
| Specimen Collection Times | | Lab Requisition form or LDMS Specimen Tracking Sheet | | | | |
| hCG | | Site-specific lab requisition form  Site testing log/results report | | | | |
| Urine dipstick/culture | | Site-specific lab requisition form  Lab results report | | | | |
| HIV-1 testing | | Site-specific lab requisition form  Site testing log/results report (rapids, Geenius confirmatory testing)  Lab result report (HIV RNA) | | | | |
| Plasma (archive/storage) | | Site-specific lab requisition form or Specimen Storage CRF, chart note, or visit checklist | | | | |
| Hepatitis B surface antigen (HBsAG) | | Site-specific lab requisition form  Lab results report | | | | |
| Blood creatinine, creatinine clearance | | Site-specific lab requisition form  Lab results report, MTN-043 Creatinine Clearance Calculator | | | | |
| AST/ALT | | Site-specific lab requisition form  Lab results report | | | | |
| CBC with platelets | | Site-specific lab requisition form  Lab results report | | | | |
| Syphilis serology | | Site-specific lab requisition form  Lab results report | | | | |
| Dried Blood Spot (DBS) for PK | | Site-specific lab requisition form, LDMS Specimen Tracking Sheet, chart note, or visit checklist | | | | |
| Plasma for DPV drug levels | | Site-specific lab requisition form, LDMS Specimen Tracking Sheet, chart note, or visit checklist | | | | |
| NAAT for GC/CT/Trich | | Site-specific lab requisition form  Lab results report | | | | |
| Wet prep/KOH wet mount with pH for candidiasis and/or BV | | Site-specific lab requisition form and/or visit checklist  Chart note or lab results report | | | | |
| Vaginal swab for microbiota | | Site-specific lab requisition form, LDMS Specimen Tracking Sheet, chart note, or visit checklist | | | | |
| Vaginal swab for biomarkers | | Site-specific lab requisition form, LDMS Specimen Tracking Sheet, chart note, or visit checklist | | | | |
| Vaginal Gram Stain | | Site-specific lab requisition form, LDMS Specimen Tracking Sheet, chart note, or visit checklist | | | | |
| Breast milk for DPV drug levels and FTC & TFV drug levels | | Site-specific lab requisition form, LDMS Specimen Tracking Sheet, chart note, or visit checklist | | | | |
| Returned Study VR | | Site-specific lab requisition form, LDMS Specimen Tracking Sheet, chart note, or visit checklist | | | | |
| **STUDY PRODUCT/ SUPPLIES** | | | | | | |
| Provision of study VR or tablets | | Study Prescription (initial product request to pharmacy)  Study Product Request Slip  Site-specific Pharmacy Dispensing Log (source for dispensations from pharmacy)  Pharmacy Dispensation CRF  Ring Insertion and Removal CRF, PrEP Provisions and Returns and/or chart notes and/or Site-Specific Clinic Study Product Accountability Log | | | | |
| Provision of study product instructions | | Chart note, visit checklist, and/or site-specific document | | | | |
| Insertion/ingestion of the provided study product (first product use) | | Ring Assessment CRF or Tablet Assesment CRF | | | | |
| Digital/Visual exam(s) by clinician to check VR placement | | Chart note or visit checklist | | | | |
| Removal and collection of used/unused study product | | Ring Insertion and Removal CRF  PrEP Provisions and Returns CRF  Specimen Storage CRF (Vaginal Ring)  LDMS Tracking Sheet (Vaginal Ring)  Chart note or visit checklist | | | | |
| Offer condoms | | Site-specific counseling notes/worksheets or visit checklist | | | | |
| **OTHER** | | | | | | |
| Protocol Deviations | | Protocol Deviation Log CRF | | | | |
| A record of all contacts, and attempted contacts, with the participant | | Missed Visit CRF  Site-specific contact/outreach/retention logs and/or chart notes | | | | |
| A record of all procedures performed by study staff during the study | | Visit checklists, chart notes, and/or other site-specific flow sheets | | | | |
| Staff-initiated Study Product Discontinuations/Holds | | Discontinuation of Study Product CRF  Product Hold Y/N and Log CRF  Chart notes and/or pharmacy request slip | | | | |
| A record of participant’s exit from the study | | Study Termination CRF  Chart notes | | | | |

**Appendix 1: Part B**

**MTN-043 CRFs and Source Documents**

|  |  |  |
| --- | --- | --- |
| **CRF Name** | **Is eCRF Source?** | **Comments**  *(Unless otherwise noted in the Comments column, the CRF is source for all form items.)* |
| Adverse Events Y/N | Yes | Form is administrative only. |
| Adverse Event Log | Mixed | * Form is source for participant reported AEs * Non-CRF documents are source for Laboratory and Clinical AEs |
| Additional Study Procedures | Yes | Form is administrative only. |
| Infant Additional Study Procedures | Yes | Form is administrative only. |
| Baseline Medical History Y/N | Yes | Form is administrative only. |
| Baseline Medical History Log | Mixed | Form may be source for all items or source may be medical records, if available. Supplemental information may also be recorded in chart notes. |
| Chemestry Panel | No | Non-CRF lab source document (report or testing log) is source |
| Concomitant Medications Y/N | Yes | Form is administrative only. |
| Concomitant Medications Log | Mixed | Form may be source for all items or source may be medical records, if available. Supplemental information may also be recorded in chart notes. |
| Demographics | Yes | Form is source for all items as participant responses are entered directly into the form. |
| Infant Demographics | Mixed | Form may be source for all items or source may be medical records, if available. Supplemental information may also be recorded in chart notes. |
| Discontinuatiuon of Study Product | Yes |  |
| Edinburgh Postnatal Depression Scale | Yes |  |
| Enrollment | Mixed | Randomization information from Medidata Balance is source for study arm. |
| Feeding Assessment – Screening and Enrollment | Yes | Participant responses are entered directly into the form. |
| Feeding Assessment – Follow Up | Yes | Participant responses are entered directly into the form. |
| Feeding Inventory | Yes | Participant responses are entered directly into the form. |
| Follow-up Y/N | Yes | Form is administrative only. |
| Follow-up Visit Summary | Yes | Form is administrative only. |
| Infant Follow-up Visit Summary | Yes | Form is administrative only. |
| Hematology | No | Non-CRF lab source document (report or testing log) is source |
| HIV Test Results | No | Non-CRF lab source document (report or testing log) is source |
| HIV Confirmatory Results | Mixed | Form is source for final HIV status. Non-CRF lab source document (report or testing log) is source for other items. |
| Infant HIV Confirmatory Results | Mixed | Form is source for final HIV status. Non-CRF lab source document (report or testing log) is source for other items. |
| IDI Tracking | Yes | Form is administrative only. |
| Inclusion/ Exclusion Criteria | No | Screening Behavioral Eligibility Worksheet, Enrollment Behavioral Eligibility Worksheet, Eligibility checklist and/or Screening and Enrollment Log is source for all items. |
| Infant Inclusion/ Exclusion Criteria | No | Screening Behavioral Eligibility Worksheet, Enrollment Behavioral Eligibility Worksheet, Eligibility checklist and/or Screening and Enrollment Log is source for all items. |
| Infant Ages and Stages Assessment | Mixed | Paper Infant Ages and Stages Questionnaires are source for total scores. CRF may be source for identified abnormalies. |
| Informed Consent | No | ICF and IC coversheet or chart notes are source |
| Interim Visit Summary | Yes | Form is administrative only. |
| Infant Interim Visit Summary | Yes | Form is administrative only. |
| Missed Visit | Yes |  |
| One-Year Infant Assessment | Mixed | Form may be source for all items or source may be medical records, if available. Supplemental information may also be recorded in chart notes. |
| Participant Type | Yes | Form is administrative only. |
| Participant Identifier | Yes | Form is administrative only. |
| Pelvic Exam | No | Pelvic Exam Diagrams is source for findings. AE Log CRF is source for item ‘any new pelvic findings AEs’. |
| Pharmacy Dispensation | No | Pharmacy dispensing records and randomization information from Medidata Balance are source. |
| Physical Exam | Yes |  |
| Pregnancy Test Results | No | Non-CRF lab source document (report or testing log) is source |
| Pregnancy Report | Mixed | Form may be source for all items or source may be medical records, if available. Supplemental information may also be recorded in chart notes. |
| Pregnancy Outcome | Mixed | Form may be source for all items or source may be medical records, if available. Supplemental information may also be recorded in chart notes. |
| Pregnancy History | Yes | Form is source for all items. Supplemental information also may be recorded in chart notes. |
| Product Hold Y/N | Yes | Form is administrative only. |
| Product Hold Log | Yes |  |
| Protocol Deviations Y/N | Yes | Form is administrative only. |
| Protocol Deviation Log | Yes | Form is source for all items. Supplemental information may also be recorded in the chart notes. |
| PrEP Provisions and Returns | No | Study Product Accountability Log is source for all items |
| Randomization | Mixed | Form is source for “Is the participant ready to be randomized?” Medidata Balance is source for “Randomization Date and Time”. |
| Ring Assessment | Yes |  |
| Ring Insertion and Removal | Mixed | Study Product Accountability Log is source for ring provision/return. Other items on CRF are source. |
| Screening Date of Visit | Yes | Form is administrative only. |
| Seroconverter Results | No | Non-CRF lab source document (report or testing log) is source |
| Specimen Storage | Mixed | Form is source for “If not stored, specify reason” and “If "Breastmilk for drug concentration", what method was used to collect the breast milk sample?”. LDMS Specimen Tracking Sheet or local lab form may be source for other items. |
| Infant Specimen Storage | Mixed | Form is source for “If not stored, specify reason”. LDMS Specimen Tracking Sheet or local lab form may be source for other items. |
| Social Impact | Yes |  |
| Social Impact Y/N | Yes | Form is administrative only. |
| Social Impact Log | Yes |  |
| STI Test Results | No | Local lab report is source for all items. |
| Study Termination | Yes |  |
| Tablet Assessment | Yes |  |
| Urine Test Resuts | Mixed | Form may be source for dipstick results or site-specific lab report/log may be source. |
| Vaginal Practices | Yes |  |
| Vital Signs | Yes |  |
| Infant Vital Signs | Yes |  |

*\*In cases where it is specified that initial form completion will be done using an eCRF, but the eCRF cannot be accessed due to temporary internet outage, off-site visits or other unforeseen circumstances, paper CRF completion is acceptable as a temporary solution until eCRF access can be restored. Data from these paper CRFs should be entered into Medidata Rave once database access is restored.*

| **Appendix 1, Part C:**  **MTN-043 Site-Specific Forms Used as Source Documents** | | |
| --- | --- | --- |
| **Form Name** | **Is Form Source?** | **Comments** |
| Eligibility Checklist | Mixed | All items are based on source data recorded on other documents. Form is source for signature items. |
| IC Coversheet | Mixed | ICF is source for consent type, version, date, form is source for all other items |
| IC Comprehension Checklist | Yes |  |
| Screening and Enrollment Log | Mixed | Screening and enrollment visit documentation is source for screening and enrollment dates. Log may be source for reason not enrolled/screen failure. |
| PTID Nam Linkage Log | Yes |  |
| Behavioral Eligibility Worksheets (Screening and Enrollment) | Yes |  |
| LDMS Specimen Tracking Sheet | Yes |  |
| Medical Release Form | Yes |  |
| Local Site Specific Testing Logs (HIV, Urinalysis) | Mixed | Local lab testing sheet is source for rapid HIV test results, though results are also transcribed onto visit checklists. Visit checklists are source for others. |
| Pelvic Exam Diagrams | Yes |  |
| Site Specific Visit and Pelvic Exam Checklists | Mixed | Source completed procedures as specified in table A. |
| Counseling Worksheets (HIV Pre/Post Test and Risk Reduction Counseling Worksheet, Contraception Counseling Worksheet, Product Adherence Counseling Worksheet) | Yes |  |
| Ages and Stages Questionnaire | Yes |  |
| Locator Form | Yes |  |
| Study Prescription | Yes |  |
| Study Product Request Slip | Yes |  |
| Participant Specific Clinic Study Product Accountability Log | Yes |  |
| Qualititiave Participation Log | Mixed | Source for participant acceptance of IDI invitation. |