Section 3. Documentation Requirements

Study staff is responsible for proper collection, management, storage, quality control, and quality assurance of all study-related documentation. This section contains information on the Essential Documents that each study site must maintain throughout the study. It also contains information related to establishing adequate and accurate participant research records — commonly referred to as participant "case history records" — for MTN 004.

3.1 Essential Documents

The Division of AIDS (DAIDS) Policy *Requirements for Essential Documents in DAIDS Funded and/or Sponsored Clinical Trials* (The Division of AIDS (DAIDS) Standard Operating Procedures (SOPs) for Essential Documents and Source Documentation) specifies the essential documents that study sites must maintain for DAIDS-sponsored studies, including MTN 004. When required documents are modified or updated, the original and all modified or updated versions must be maintained. Although all required documentation must be available for inspection at any time, all documents need not be stored together in one location.

Section Appendix 3-1 presents a suggested essential documents filing structure for MTN 004. Study sites are not required to adopt the suggested structure, but are encouraged to consider it when developing their filing approach for MTN 004. Study sites also are encouraged to establish an SOP to document their filing approach. Further clarifications of the suggested filing structure are as follows:

- Essential documents may be stored in files and/or in binders. The files/binders listed in Section Appendix 3-1 may be further subdivided, consolidated, and/or re-organized if desired.

- It is recommended that a contents sheet be maintained and inserted as the first page(s) of each file/binder. Within each file/binder, it is recommended that documents be filed in ascending date order (most recent documents in front).

- To preserve blinding, certain documents related to the investigational study products will be stored in site pharmacies. A listing of essential documents to be maintained in the pharmacies is provided in Section 3.4, rather than Section Appendix 3-1.

- To facilitate routine inspection by study monitors, certain laboratory-related essential documents should be stored in the main study essential documents files/binders (see items 26-28 in Section Appendix 3-1). Other lab-related essential documents (e.g., lab SOPs) may be filed in the site's laboratory files.

- The suggested filing structure assumes that MTN 004 participant case history records will be stored separately from the other essential documents listed in Section Appendix 3-1. Section 3.3 below provides information on the required contents of these records. The suggested filing structure also assumes that the MTN 004 Screening and Enrollment Log, Participant Name-ID Number Link Log, Clinic Randomization Envelope Tracking Record, and Replacement Envelope Tracking Record (which are described in Section 4 of this manual) will be stored in the study clinic or data management area, and not necessarily with the other essential documents listed in Section Appendix 3-1.

- For the ATN sites: The Protocol Registration Policy of the Pediatric, Adolescent, and Maternal AIDS Branch (PAMAB) of the National Institute of Child Health and Human Development (NICHD) for MTN-004 Study in Section Appendix 3-8.

- For the MTN site: The DAIDS Protocol Registration Policy and Procedure Manual located at: http://rcc.tech-res.com/forms.htm.

3.2 Site Activation Requirements

After study sites have received final approval from their local Institutional Review Boards (IRB), they must submit protocol registration materials. The ATN sites will complete protocol registration with the National Institute of Child Health and Human Development (NICHD) via Westat. The MTN site will complete protocol registration with the DAIDS RCC Protocol Registration Office. For the ATN sites, when the Data and Operations Center (DOC) at Westat has received all required registration materials, and met all other activation requirements, the DOC will approve the site's protocol registration and notify the site that it may begin protocol enrollment. When the MTN site has obtained protocol registration approval and met all other activation requirements, the MTN CORE (FHI) will notify the site that it may begin protocol enrollment. Protocol registration must occur before any site can enroll any participants into the study.

The study will be conducted in full compliance with the protocol. The protocol will not be amended without prior written approval by the Protocol Chair, NIAID Medical Officer, and NICHD Medical Officer. All protocol amendments must be submitted to and approved by the relevant IRB(s), and where necessary, submitted by Starpharma to the FDA, prior to implementing the amendment.

3.3 Participant Case History Documents

Study sites must maintain adequate and accurate participant case history records containing all information pertinent to MTN 004 for each study participant.

3.3.1 Case History Contents

Participant case histories should contain all of the following elements:

- Basic participant identifiers.

- Documentation that the participant provided written informed consent to screen for and participate in the study prior to the conduct of any screening or study procedures, respectively.

- Documentation that the participant met the study's selection (eligibility) criteria. *NOTE: For participants with a vasectomized partner, self report of vasectomy will be sufficient documentation to meet the contraceptive use eligibility criterion.*

- A record of the participant's random assignment.

- A record of the participant's exposure to the investigational study products.

- A record of all contacts, and attempted contacts, with the participant.
- A record of all procedures performed by study staff during the study.
- Study-related information on the participant's condition before, during, and after the study, including:
  - Data obtained directly from the participant (e.g., interview responses and other self-reported information)
  - Data obtained by study staff (e.g., exam and lab findings)
  - Data obtained from non-study sources (e.g., non-study medical records)

In addition to the above, DAIDS requires that all protocol events (departures/deviations/violations) be documented in participant records, along with reasons for the events and measures taken to prevent or correct them, if applicable.

Note: *In addition to documenting all protocol departures/deviations/violations on site, MTN 004 study sites also must report protocol events to DAIDS and others per the MTN MOP, Section 15-4, which can be found at the following web site:*

http://www.mtnstopshiv.org/node/187

3.3.2 Concept of Source Data and Source Documentation

The International Conference on Harmonization Consolidated Guidance for Good Clinical Practice (ICH-E6) defines the terms source data and source documentation as follows:

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 documents: Original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' 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, colposcopic images, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the trial, and any other relevant documents that may be considered as participant data or records).

Source documents are commonly referred to as the documents —paper-based or electronic — upon which source data are first recorded. All study sites must adhere to the standards of source documentation specified in the DAIDS SOP for Source Documentation which can be found at http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch/Regulatory.htm). The DAIDS policy specifies both requirements and recommendations. Study sites must comply with all requirements and are encouraged, but not required, to comply with all recommendations.

For MTN 004, it is expected that participant case history records will consist of the following source documents:

- Narrative chart notes
- Clinic randomization envelopes, replacement envelopes, and prescriptions documenting participants' random assignments
- Study Gel Request Slips, Study Gel Re-supply Worksheets, Participant Replacement Assessment Worksheets
- Visit checklists
- Local laboratory testing logs and result reports
- DataFax and Non-DataFax forms provided by the MTN Statistical and Data Management Center (SDMC)
- Colposcopic images
- Other source documents (e.g., site-specific worksheets, non-study medical records)

As a condition for study activation, each study site must establish an SOP for source documentation that specifies the use of the above-listed documents as source documents. Although it is the responsibility of each site to determine the most appropriate source document for each required case history element, Section Appendix 3-2 provides a guide that sites may follow for this study. Supplemental information on the use of chart notes, visit checklists, and forms provided by the MTN SDMC is provided below. Detailed information on proper completion, maintenance, and storage of participant randomization and product dispensing documentation is provided in Sections 4, 6, and 9 of this manual. Detailed information on proper completion of DataFax and Non-DataFax forms provided by the MTN SDMC is provided in Section 14 of this manual.

Chart Notes: Study staff must document every contact with a study participant in a signed and dated chart note specifying the date, type, purpose, and location of the contact, and the general status of the participant. The time and location at which a contact takes place, as well as which particular procedures take place, should be specified when necessary to document adherence to protocol requirements. Chart notes also must be used to document the following:

- The screening and enrollment informed consent processes (see also Section 5)
- Procedures performed that are not recorded on other source documents
- Pertinent data about the participant that are not recorded on other source documents
- Protocol events that are not otherwise captured on other source documents

Study sites are strongly encouraged to adopt a common format — such as the Subjective-Objective-Assessment-Plan (SOAP) format — for all chart notes, to help ensure adequacy and consistency of note content and maximize adherence to GCP standards. Several sample notes in SOAP format are provided in Section Appendix 3-3.

Visit Checklists: The checklists in Section 7 of this manual represent convenient tools to fulfill the requirement of documenting all study procedures performed with each study participant. Note, however, that checklists alone may not be sufficient for documenting all procedures. For example, chart notes may be required to document procedures performed at unscheduled study visits, and/or to explain why procedures in addition to those listed on a checklist may have been performed or why procedures listed on a checklist were not performed. Chart notes also may be required to document the content of counseling sessions and/or other in-depth discussions with participants (e.g., related to adherence to protocol requirements).

DataFax and Non-DataFax Forms Provided by the MTN SDMC: The case report forms for this study are designed for use with the DataFax data management system described in Section 14 of this manual. The SDMC will provide these forms to each site. The SDMC also will provide several study-specific non-DataFax forms to each site. See Section Appendix 3-4 for a listing of all DataFax and non-DataFax forms to be provided for this study.

For each site, forms that are administered directly to participants will be available in local languages relevant to the site. The SDMC will provide each site with Screening files (containing Screening and Enrollment Visit forms) and Participant Study Notebooks (with separate visit tabs containing the forms needed for a given participant and study visit).
As shown in Section Appendices 3-5 and 3-6, many of the DataFax and non-DataFax forms provided by the SDMC have been designed to serve as source documents. Before the study starts, each study site must identify the forms that routinely will be used as source documents in its SOP for source documentation, and must follow the specifications of this SOP consistently for all study participants. In the event that study staff is not able to record data directly onto forms designated as source documents per the site Source Documentation SOP, the following procedures should be undertaken:

- Record the data onto an alternative source document
- Enter the alternative source document into the participant's study chart
- Transcribe the data from the alternative source document onto the appropriate form
- Enter a chart note stating the relevant study visit date and the reason why an alternative source document was used

3.3.3 Document Organization

All information pertaining to the participants (including a case history) must be stored in the same manner for all study participants. Study staff must store all study records securely and confidentially in areas with access limited to authorized study staff only (see Protocol Section 13.5 Participant Confidentiality). Study staff is responsible for purchasing file folders, binders, storage cabinets, and any other equipment or supplies needed to properly store all records.

Study-related documentation collected during the screening process should be stored in file folders or thin notebooks for each potential participant. All screening documentation — for potential participants who eventually enroll in the study as well as for those who do not enroll — must be maintained and available for monitoring throughout the study. For participants who enroll in the study, screening documentation (from successful screening attempt that led to enrollment *only*) should be transferred into SDMC-provided participant notebooks, which will serve as participants' study notebooks for the duration of their participation in the study.

All documents contained in participant case history records must bear a participant identifier, which generally will consist of either the participant identification number (PTID) or the participant name. To maximize participant confidentiality, the PTID should be used whenever possible, and records that bear names or other personal identifiers, such as locator forms and informed consent forms, should be stored separately from records identified by PTID. Any documents transferred or transmitted to a non-study site location — including DataFax forms and Expedited Adverse Event Forms — must be identified by PTID only.

Regardless of whether the identifier on a particular document consists of the participant name or PTID, 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 PTID 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 notebooks and/or transferred or transmitted to the DAIDS and NICHD Medical Officers.

Copies of source documents may not be transferred to any other non-study site location without prior authorization from the DAIDS and NICHD Medical Officers or the CORE (FHI) Clinical Research Manager (or their designees).

All on-site databases must be secured with password-protected access systems. Any lists, logbooks, appointment books, or other documents that link PTIDs to other participant identifiers must be stored securely in a location separate from records identified by either participant name only or PITD only. When in use, these documents must not be left unattended or otherwise accessible to study participants, other study clinic patients, or any other unauthorized persons.

As a condition for study activation, each study site must establish an SOP for data management. This SOP minimally should contain the following elements:

- Procedures for assigning PTIDs, linking PTIDs to participant names, and storing the name-PTID link log
- Procedures for establishing participant files/charts/notebooks
- During-visit participant chart and case report form review procedures
- Post-visit participant chart and case report form review procedures and timeframes
- Data transmission procedures, including timeframes, case report form storage locations before and after faxing, and mechanisms for identifying when forms have been transmitted
- Procedures for resolving data quality control notes from the SDMC

- Procedures for handling and filing field workers' logs, worksheets, etc.
- Storage locations for blank case report forms
- Storage locations for documents identified by participant names or other personal identifiers
- Storage locations for documents identified by PTID
- Procedures for back up of electronic study data (if applicable)
- Handling of participant study records for off-site contacts and visits
  (*Note:* For MTN 004, study visits may **not** be conducted off-site)
- Confidentiality protections
- Other ethical and human subjects considerations
- Staff responsibilities for all of the above (direct and supervisory)
- Staff training requirements (if not specified elsewhere)
- QC/QA procedures related to the above (if not specified elsewhere)

3.4 Study Product Accountability, Chain of Custody, and Dispensing Documentation

The following essential documents should be maintained in study site pharmacies:

- Current MTN 004 protocol
- Current Investigator's Brochure (IB) VivaGel™ (if IB on file in the clinic essential document files are not easily accessible to pharmacy staff)
- Current MTN 004 FDA Form 1572
- Current list of authorized prescribers and staff authorized to sign MTN 004 Study Product Request Slips (names and signatures)
- Pharmacy Establishment Plan
- MTN 004 pharmacy and product-related SOPs
- MTN 004 PTID list (provided by the MTN SDMC)
- MTN 004 product shipping and receipt documentation
- MTN 004 product storage temperature logs
- MTN 004 investigational agent accountability records
- MTN 004 participant-specific records (including prescriptions, product re-supply slips, dispensing records, and DataFax forms as applicable)
- MTN 004 monitoring visit reports
- MTN 004 communications with site clinic staff
- MTN 004 communications with the MTN CORE Pharmacist and Brecon
- MTN 004 communications with the MTN Coordinating and Operations Center (CORE)
- MTN 004 communications with the MTN SDMC
- Other MTN 004 communications
- Other locally-required administrative, operational, and/or regulatory documentation
- MTN 004 drug destruction log or return shipment log

Pharmacy staff will document the receipt, dispensing, and final disposition of the investigational products used in the study (i.e., VivaGel™ , VivaGel™ placebo gel, and HEC placebo gel).

Pharmacy staff also will maintain in the study pharmacies Participant-Specific Pharmacy Dispensing Records containing information on product dispensations for all enrolled participants. Study clinic staff will contribute to the documentation of product dispensation and chain of custody as described in Sections 4, 6, and 9 of this manual.

The specifications related to document security and participant confidentiality described in Section 3.3.3 also apply to records maintained in the study pharmacies. All records must be stored securely in the pharmacies with access limited to authorized study pharmacy staff only.

To preserve the blinding of all protocol team members to participants' random assignments to study gel (VivaGel™, VivaGel™ placebo gel or HEC placebo gel), neither the study clinic staff, study participants, nor the MTN 004 team members will be provided access to product-related documentation maintained in the study pharmacies. Pharmacy staff may provide copies of some participant-specific documentation maintained in the study pharmacies (e.g., chart notes) to clinic staff for purposes of communication and operational coordination. However, decisions to provide such documentation to clinic staff will be made by pharmacy staff only, and under no circumstances will documentation released from the pharmacy include participants' product dispensing records.

Note: Double blinding of non-pharmacy site staff will only pertain to random assignment, and not frequency of study gel use. All site study staff will remain unblinded to participants' frequency of study gel use.

3.5 Record Retention Requirements

All records must be retained on-site throughout the study's period of performance. In accordance with U.S. regulations, all study records will be retained until NICHD, DAIDS and Starpharma give approval for record destruction. Study product records must be stored in the study pharmacies, with access limited to authorized study pharmacy staff only, until the study is unblinded. DAIDS will provide further instructions for long-term storage of study records after the study is completed.

Section Appendix 3-1
Suggested Filing Structure for MTN 004 Essential Documents

File/Binder #1: MTN 004 Protocol and Current Informed Consent Forms 1. MTN 004 Protocol (including copy of signed and dated protocol signature page): Version 1.0, 2.0 and 3.0 and any subsequent protocol Clarification Memos, Letters of Amendment, and Amendments 2. Currently-approved MTN 004 informed consent forms
File/Binder #2: Regulatory Authority Documentation (if applicable) 3. Regulatory Authority Correspondence/Authorization/Approval/Notification of Protocol (if applicable; if more than one regulatory authority has oversight responsibility for research performed at the study site, include subsections for each authority)
File/Binder #3A: IRB/EC Documentation for [IRB/EC A] 4. FWA documentation for IRB/EC A 5. Roster of IRB/EC A (if available) 6. Relevant IRB/EC A Submission Requirements/Guidelines/SOPs 7. IRB Correspondence for IRB/EC A: File complete copies of all correspondence to and from the IRB/EC; include all enclosures/attachments for all submissions, even if copies of the enclosures/attachments are filed elsewhere; include all approval documentation.
File/Binder #3B: IRB/EC Documentation for [IRB/EC B] 8. FWA documentation for IRB/EC B 9. Roster of IRB/EC B (if available) 10. Relevant IRB/EC B Submission Requirements/Guidelines/SOPs 11. IRB Correspondence for IRB/EC B: File complete copies of all correspondence to and from the IRB/EC; include all enclosures/attachments for all submissions, even if copies of the enclosures/attachments are filed elsewhere; include all approval documentation.
File/Binder #4: Product Safety Information 12. Investigator's Brochure for VivaGel gel: current version and any subsequent updates 13. Product Safety Information/Reports/Memos Notes: • It is assumed that expedited adverse event reports will be stored in participant study notebooks. • It is assumed that documentation of IRB/EC submission of above-listed documents (if applicable) will be maintained in the relevant IRB/EC Files/Binders (i.e., File/Binder #3A and #3B).
File/Binder #5: MTN 004 Study-Specific Procedures (SSP) Manual 14. Final version 1.0 and any subsequent updates Notes: For this reference copy of the SSP Manual, do not discard out-dated pages or sections when updates are issued; retain all versions of all pages as a complete historical record. • The SSP Manual contains reference versions of all study case report forms, therefore additional (blank) copies of the case report forms need not be stored elsewhere in the essential document files.
File/Binder #6: MTN 004 Study-Specific Standard Operating Procedures 15. Final approved version of each SOP, and any subsequent updates to each

Section Appendix 3-1
Suggested Filing Structure for MTN 004 Essential Documents

File/Binder #7: MTN 004 Staffing Documentation

16. FDA Form 1572 (the original form should be submitted to Starpharma a copy of the form submitted for Protocol Registration, and any subsequent updates)
17. MTN 004 Investigator of Record CV (copy of CV submitted for Protocol Registration; ensure that the CV is current prior to initiating MTN 004; it is recommended that CVs be signed and dated to document at least annual updating)
18. Financial Disclosure Forms (original signed and dated forms, and any subsequent updates)
19. Study Staff Roster (copies submitted to Westat, if applicable, and FHI for study activation, and any subsequent updates)
20. Study Staff Identification and Signature Sheet (if not combined with staff roster; copies and any subsequent updates)
21. Study Staff Delegation of Duties (if not combined with staff roster; copies and all updates)
22. CVs for Study Staff other than the IoR (ensure that all CVs are current prior to initiating MTN 004; it is recommended that CVs be signed and dated to document at least annual updating)
23. Study Staff Job Descriptions
24. Documentation of Study Staff Training

File/Binder #8: Local Laboratory Documentation

25. Local Laboratory Certification(s), Accreditation(s) and/or Validation(s): file documentation current at time of study activation and all subsequent updates
26. Local Laboratory Normal Ranges: file documentation of relevant normal ranges for all protocol-specified tests current at time of study activation and all subsequent updates
27. Laboratory Manager CV (or cross-reference to CV contained in File/Binder #7)

Note:

- It is recommended that a cross-reference be included in this file/binder specifying the storage location(s) of other lab-related essential documents filed in the local lab(s).

File/Binder #9: Monitoring Visit Documentation

28. Monitoring Visit Log
29. Initiation and Monitoring Visit Reports and Documentation of Response to Visit Findings

File/Binder #10: Documentation of Other MTN Site Visits

30. (Non-Monitoring) Site Visit Log
31. MTN CORE Site Visit Reports and Documentation of Response to Visit Findings
32. MTN SDMC Site Visit Reports and Documentation of Response to Visit Findings
33. MTN Network Lab Site Visit Reports and Documentation of Response to Visit Findings
34. Other Site Visit Reports and Documentation of Response to Visit Findings

File/Binder #11: Study-Related Sponsor Communications

35. Study-Related Communications to and from DAIDS
36. Study-Related Communications to and from NICHD

Notes:

- Communications should be filed beginning from the date of the MTN 004 site specific Training.
- Communications related to individual MTN 004 study participants will be filed in individual participant study records.
- As needed to preserve blinding, product-related communications will be stored in the study pharmacy.

Section Appendix 3-1
Suggested Filing Structure for MTN 004 Essential Documents

File/Binder #12: Other Study-Related Communications

37. Study-Related Communications to and from MTN CORE
38. Study-Related Communications to and from MTN SDMC
39. Study-Related Communications to and from MTN Network Lab
40. Other Study-Related Communications

Notes:

- Communications should be filed beginning from the date of the MTN 004 site specific training.
- Communications related to individual MTN 004 study participants will be filed in individual participant study records.
- As needed to preserve blinding, product-related communication will be stored in the study pharmacy.

File/Binder #13: Study Site Staff Meeting Documentation

41. MTN 004 Staff Meeting Agendas, Participant Lists/Sign-In Sheets, and Summaries

Note:

- Meeting documentation should be filed beginning from the date of the MTN 004 site specific training.

File/Binder #14: Conference Call Documentation

42. MTN 004 Protocol Team Conference Call Summaries
43. Summaries of Other MTN 004 Conference Calls

Note:

- Conference call summaries will be filed beginning from the date of the MTN 004 site specific training.

File/Binder #15: DAIDS and Other Reference Documentation

44. DAIDS Policy *Requirements for Source Documentation at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials* (Version 2.0 and any subsequent updates)
45. DAIDS Policy *Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials* (Version 2.0 and any subsequent updates)
46. ATN sites: The Protocol Registration Policy of the Pediatric, Adolescent, and Maternal AIDS Branch (PAMAB) of the National Institute of Child Health and Human Development (NICHD) for the MTN 004 Study (Version 0.5, February 2007 and any subsequent updates)
47. MTN sites: DAIDS Protocol Registration Policy and Procedures Manual (August 2004 and any subsequent updates)
48. Manual for Expedited Reporting of Adverse Events to DAIDS
49. US Regulations Applicable to Conduct of MTN 004 (45 CFR 46; 21 CFR 50, 54, 56, and 312)
50. Any other relevant manuals or reference documents

File/Binder #16: Site-Specific Study Activation Documentation

50. Site-Specific Study Activation Documents

Section Appendix 3-2
Guide to Required Case History Elements and Source Documents for MTN 004

Required Case History Element	Source Documents*
Basic participant identifiers.	Locator form; Demographics forms.
Documentation that the participant provided written informed consent to screen for and participate in the study.	Signed and dated informed consent forms; signed and dated chart notes stating that informed consent was obtained prior to initiating study procedures.
Documentation that the participant met the study selection (eligibility) criteria.	Demographics form, locator form; Screening 1 Visit Eligibility form (non-DataFax); Screening 2 Visit/Enrollment Eligibility form (non-DataFax), Screening Summary (non-DataFax); Clinical Eligibility form (non-DataFax); Safety Laboratory Results form; STI Laboratory Results form; (non-DataFax) Baseline Medical History form; Concomitant Medications Log form; Physical Exam form (non-DataFax); Screening 1 and Enrollment Pelvic Exam form; Screening 2 Pelvic exam form (if indicated); (non-DataFax) Pelvic Exam Diagrams; Pelvic Laboratory Results form; Enrollment form; Pre-Existing Conditions form; local lab logs and result reports[§]; signed and dated chart notes.
A record of the participant's random assignment.	MTN 004 prescription or MTN 004 replacement prescription; MTN 004 Participant-Specific Pharmacy Dispensing Record; Enrollment form; dispensed gel chain of custody logs.
A record of the participant's exposure to the investigational study products.	MTN 004 Gel Re-Supply Worksheet, MTN 004 Study Gel Request Slip, MTN 004 Participant-Specific Pharmacy Dispensing Record; dispensed gel chain of custody logs, visit checklists.
A record of all contacts, and all attempted contacts, with the participant.	Signed and dated chart notes, and/or other worksheets or site-specific documents if designated in site SOPs.
A record of all procedures performed by study staff.	Completed visit checklists; signed and dated chart notes detailing (i) procedures performed in addition to those contained on the checklist and/or (ii) the reason why procedures contained on the checklist were not performed.

Information on the participant's condition before, during, and after the study.	All documents listed above; Family Planning Methods form, Study Gel Adherence form; Acceptability Assessment form; (non-DataFax) Follow-up Medical History form; Genital Bleeding Assessment; Follow-up Pelvic Exam form; (non-DataFax) Pelvic Exam Diagrams; (non-DataFax) History of Genital Symptoms form; Baseline Genital Symptoms form; Follow-up Genital Symptoms form; Pharmacokinetics form; Pelvic Laboratory Results form; Safety Laboratory Results form; STI Laboratory Results form; HSV-2 Culture form; Adverse Experience Log form; HIV Test Results form; Product Hold/Discontinuation form; Pregnancy Report and History form; Pregnancy Outcome form; Missed Visit form; Follow-Up Visit form; Interim Visit form; End of Study Inventory form; local lab logs and result reports from the local lab[§]; results of information pertinent to the study obtained from non-study sources; signed and dated chart notes.

*Other site-specific source documents also may be used.
[§]A clinician must review all local laboratory reports and document this review by signing and dating all reports.

Sample Chart Note for a Screening Visit:

15 AUG 2008: Participant presented for MTN 004 screening. Obtained written informed consent for screening before initiating any procedures. Procedures were completed per protocol, visit checklist and SOPs.

S: Participant reported no current health problems.

O: Pregnancy test negative, participant behaviorally eligible per the Screening Eligibility form, HIV test sent to lab.

A: Participant is eligible for the study thus far.

P: Screening visit 2 and Enrollment scheduled for 01 SEP 2008.

{staff signature}

Sample Chart Note for a Screening Visit:

15 AUG 2008: Participant presented for MTN 004 screening. Obtained written informed consent for screening before initiating any procedures. Procedures were completed per protocol, SOPs and visit checklist, with the additions listed here.

S: Participant complained of current genital itching and yellowish discharge, no other current health problems.

O: Participant behaviorally eligible per the Screening 1 Visit Eligibility form, tested negative for pregnancy HIV test sent to lab.

A: Syndromic treatment provided. Participant instructed that she is not eligible to enroll in the study.

P: Participant counseled to contact her primary care provider if symptoms do not resolve in 5-7 days.

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Sample Chart Note for Screening:

15 AUG 2008: Participant presented for MTN 004 screening. Obtained written informed consent for screening before initiating any procedures. Procedures were completed per protocol, SOPs and the visit checklist, with the additions listed here.

S: Participant complained of current genital itching and yellowish discharge.

O: Participant behaviorally eligible per the Screening 1 Visit Eligibility form, tested negative for pregnancy, and HIV test sent to lab. Pelvic exam completed to assess genital symptoms. Discharge noted, but no abdominal tenderness or other signs present. Wet prep was positive for trichomonads, negative for whiff test, clue cells, and yeast.

A: Treatment provided. Participant instructed that she is not eligible to enroll in the study.

P: Participant counseled to contact her primary care provider if symptoms do not resolve in 5-7 days.

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Sample Chart Note for Enrollment:

29 AUG 2008: Participant presented for MTN 004 Enrollment visit. Procedures completed per protocol, visit checklist and SOPs. Participant was confirmed eligible and willing to take part in study. Written informed consent obtained for enrollment before initiating any study procedures. Participant was not willing to consent to specimen storage for possible future research.

S: Participant reported no genital symptoms since last visit (screening).

O: Screening 1 Visit GC and CT tests were negative. Today's pregnancy test was negative. Pelvic exam and wet mount were normal (see findings on DataFax forms). Participant behaviorally eligible per Screening 1 Visit and Screening 2 Visit/Enrollment Eligibility form. Screening documentation reviewed and eligibility confirmed by [insert name]. {counter-signature}

A: Participant is eligible for the study.

P: Participant was enrolled in study. Week 1 visit scheduled for 05 SEP 2008.

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Sample Chart Note for Enrollment Visit:

29 AUG 2008: Participant presented for MTN 004 Enrollment visit. Procedures completed per protocol, SOPs and visit checklist. Enrollment procedures were discontinued at this visit due to participant ineligibility.

S: Participant reported no current health problems.

O: Screening 1 GC and CT lab tests were negative, but today's pregnancy test was positive. Enrollment discontinued upon finding this result.

A: Participant is pregnant — not eligible for study.

P: Participant informed that she is pregnant and referred to [clinic name] for antenatal care. Participant informed that she can return to find out about study participation when she is no longer pregnant.

{staff signature}

Sample Chart Note for Follow-up Visit:

04 SEP 2008: Participant presented for MTN 004 at Week 1 visit. Procedures completed per protocol, visit checklist and SOPs.

S: No issues/problems reported since last visit.

O: Pregnancy test negative.

A: No issues of concern.

P: Week 2 visit scheduled for 11 SEP 2008.

{staff signature}

MTN 004 DataFax Forms		**MTN 004 Non-DataFax Forms**
Screening Consent		Screening 1 Visit Eligibility
Demographics		Screening 2 Visit/Enrollment Eligibility
Pharmacokinetics		Follow-up Medical History
Screening 1 and Enrollment Pelvic Exam		Baseline Medical History
Screening 2 Pelvic Exam		History of Genital Symptoms
Follow-up Pelvic Exam		Screening Summary
Enrollment		Pelvic Exam Diagrams
STI Laboratory Results		Clinical Eligibility
Pelvic Laboratory Results		Physical Exam
Safety Laboratory Results		
HSV-2 Culture		
HIV Test Results		
Pre-Existing Conditions		
Concomitant Medications Log		
Baseline Genital Symptoms		
Follow-up Genital Symptoms		
Follow-up Visit		
Genital Bleeding Assessment		
Family Planning Methods		
Study Gel Adherence		
Acceptability Assessment		
Product Hold/Discontinuation		
Adverse Experience Log		
Pregnancy Report and History		
Pregnancy Outcome		
Interim Visit		
Missed Visit		
CASI Tracking		
Termination		
End of Study Inventory		

Section Appendix 3-5
Use of MTN 004 DataFax Forms as Source Documents

Form Name	Acronym	Source?	Comments
Screening Consent	SC-1	[No]	Form [may be] source for item 1. Items 2 and 2a are based on source data recorded in participant chart notes and on participant informed consent forms.
Demographics	DEM-1	Yes	Form is interviewer-administered; participant responses are recorded directly onto the form.
STI Laboratory Results	SLR-1	[No]	Items 1f-3b1 require local lab documentation as source. Items 4a-4b require central lab documentation as source. For items 1a-1e, form may serves as source in cases where results are not documented on a local lab report, but are recorded directly onto the form. Otherwise, the local laboratory report may serve as source.
Safety Laboratory Results	SL-1-2	[Mixed]	Local laboratory report is source for items 1-5b. Form may be source for item 6.
HSV-2 Culture	HSR-1	No	Local laboratory report is source.
Screening 1 and Enrollment Pelvic Exam	SPE-1,2	[Yes]	[It is expected that this form routinely will serve as a source document, with supplemental information recorded on the Pelvic/Colposcopy Diagrams, and in participant chart notes if needed. If, instead, other documents such as participant chart notes routinely will serve as the source document for pelvic exam information, this should be specified.]
Screening 2 Pelvic Exam	RSP-1	[Yes]	[It is expected that this form routinely will serve as a source document, with supplemental information recorded on the Pelvic/Colposcopy Diagrams, and in participant chart notes if needed. If, instead, other documents such as participant chart notes routinely will serve as the source document for pelvic exam information, this should be specified.]
Pelvic Laboratory Results	PLR-1	[Mixed]	For items 1a-1f, form may serve as source in cases where results are not documented on a local lab report, but are recorded directly onto the form. Otherwise, the local laboratory report may serve as source. Local laboratory report is source for item 2.
Baseline Genital Symptoms	BGS-1	Yes	Form is interviewer-administered; participant responses are recorded directly onto the form.
Follow-up Genital Symptoms	FGS-1	Yes	Form is interviewer-administered; participant responses are recorded directly onto the form.

Section Appendix 3-5 (continued) Use of MTN 004 DataFax Forms as Source Documents			
Form Name	**Acronym**	**Source?**	**Comments**
Pre-Existing Conditions	PRE-1	No	All items are based on source data recorded on the Baseline Medical History, Physical Exam, Screening and Enrollment Pelvic Exam forms, Pelvic Exam Diagrams, Baseline Genital Symptoms, and/or participant chart notes.
Concomitant Medications	CM-1	[Yes]	[It is expected that sites will record concomitant medication information directly and initially onto this form, with the exception of family planning/contraceptive use, for which the Baseline Medical History and Follow-up Medical History forms will be source. If instead other documents such as participant chart notes routinely will serve as the source document for this information, then this form is not considered a source document, and the actual source document should be specified here.]
Enrollment	ENR-1	Mixed	Items 1 and 1a are based on source data recorded in participant chart notes and on participant informed consent forms. For items 2, 2b, and 2c, this form may serve as source, or the Clinic Randomization Envelope Tracking Record may serve as source (depending on which is completed first). Items 2a, 2d, and 2e are based on source data recorded on the prescription contained inside the participant's randomization envelope. For item 3, participant chart notes, this form, or the prescription may serve as source. For item 2f the prescription of the participant being replaced serves as source. Items 4-6 are based on source data documented on the Participant-Specific Pharmacy Dispensing Record (stored in the site pharmacy).
Family Planning Methods	FPM-1	No	Responses transcribed from Baseline Medical History form at enrollment and from Follow-up Medical History form during follow-up.
Study Gel Adherence	SGA-1	Yes	Form is interviewer-administered; participant responses are recorded directly onto the form.
Follow-up Visit	FV-1	Mixed	Form may serve as source for item 1 if result is not documented on a local lab report or local log sheet, but is recorded directly onto the form. Form may also serves as source for items 1a, and 3. Participant chart notes and/or AE Log forms are source for items 2-2a. The Participant-Specific Pharmacy Dispensing Record serves as source for items 5-5b.

Section Appendix 3-5 (continued) Use of MTN 004 DataFax Forms as Source Documents			
Form Name	**Acronym**	**Source?**	**Comments**
Follow-up Pelvic Exam	FPE-1-3	[Yes]	[It is expected that this form routinely will serve as a source document, with supplemental information recorded on the Pelvic/Colposcopy Diagrams, and in participant chart notes if needed. If, instead, other documents such as participant chart notes routinely will serve as the source document for pelvic exam information, this should be specified.]
HIV Test Results	HTR-1	[No]	Local laboratory report is source for items 1-4. Local laboratory report and/or form may serve as source for item 5.
Acceptability Assessment	AA-1-5	Yes	Form is interviewer-administered; participant responses are recorded directly onto the form.
Pharmacokinetics	PK-1	[Yes]	Form may serve as source for items 1, 4 and 5. Form may also serve as source for items 2-3 if height and weight are re-assessed at the time of the PK visit, and recorded directly onto this form. The Physical Exam form and/or participant chart notes may also serve as source for items 2-3.
Product Hold/Discontinuation	PH-1	Mixed	Form may be source for all items EXCEPT item 2. Participant chart notes, the PR-1 form, local laboratory report and/or local log sheet, HTR-1 form, and/or AE Log form may serve as source for item 2.
Adverse Experience Log	AE-1	Yes	Form may be source for all items.
Pregnancy Report and History	PR-1	Mixed	Form may be source for item 2. All other items are based on source data recorded on the Baseline and Follow-up Medical History forms.
Pregnancy Outcome	PO-1	Yes	Form may be source for all items if medical records are not available and the data recorded on the form are based on participant self-report.
Genital Bleeding Assessment	GBA-1-3	Mixed	Follow-up Medical History form is source for items 1-3, 12, and 13. Form may be source for items 4-11g, 12a-12b, and 13a-14a. The Adverse Experience Log is source for item 14b.
Interim Visit	IV-1	Mixed	Form may serve as source for items 1-1f, 2a, and 3-4. Form may serve as source for item 2 if result is not documented on a local lab report or local log sheet, but is recorded directly onto the form. The Participant-Specific Pharmacy Dispensing Record serves as source for items 6-6b.
Missed Visit	MV-1	Yes	Form may be source to document that the visit was missed; source data on the reason why the visit was missed also may be recorded on this form.
CASI Tracking	CT-1	Yes	Form may be source for all items.
Termination Form	TM-1	No	All items are based on source data recorded on other documents.
End of Study Inventory	ESI-1	No	All items are based on source data recorded on other documents.

Section Appendix 3-6

Use of MTN 004 Non-DataFax Forms as Source Documents

Form Name	Source?	Comments
Screening 1 Visit Eligibility	Mixed	Screening Informed Consent form is source for item 1. The Screening and Enrollment Log is source for item 2. Form may serve as source for item 3 if documentation of a normal Pap result (in the 12 calendar months prior to screening) is NOT available. Form is source for items 4-25; items are interviewer-administered. Form may be source for item 26 if result is not documented on a local laboratory report or local log sheet, but is recorded directly onto the form. Form may also be source for item 27.
Screening 2 Visit/Enrollment Eligibility	Mixed	Form is source for items 1-13a; items are interviewer-administered. Form may be source for item 14, if result is not documented on a local laboratory report or local log sheet, but is recorded directly onto the form. Form may be source for item 15.
Baseline Medical History	Yes	Form may be source for all items. Data recorded on this form is based on participant self-report, and may also be supplemented with data recorded on other source documents (e.g., non-study medical records).
History of Genital Symptoms	Yes	Form may be source for all items. Data recorded on this form is based on participant self-report, and may also be supplemented with data recorded on other source documents (e.g., non-study medical records).
Physical Exam	Yes	Form may be source for all items.
Pelvic Exam Diagrams	Yes	Form may be source for all items.
Clinical Eligibility	No	All items are based on data recorded on other documents as source.
Screening Summary	No	All items are based on data recorded on other documents as source.
Follow-up Medical History	Yes	Form may be source for all items.

THE PROTOCOL REGISTRATION POLICY OF THE PEDIATRIC, ADOLESCENT, AND MATERNAL AIDS BRANCH (PAMAB) OF THE NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)

FOR THE

Microbicide Trials Network (MTN) 004 Study

Version 0.5, February 2007

6.1 Background

The Pediatric, Adolescent, and Maternal AIDS Branch (PAMAB–"Program") of the National Institute of Child Health and Human Development (NICHD), as a Branch in a Federal agency (U.S. Department of Health and Human Services–DHHS) that funds clinical research, is responsible for ensuring that the MTN 004 research protocol is conducted in accordance with the Memorandum of Understanding between the MTN and the ATN all governing regulations, policies, and procedures of the DHHS, the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA). PAMAB/NICHD has established this registration policy to meet its responsibility. PAMAB/NICHD has further delegated to the ATN Data and Operations Center (ATN-DOC) the task of collecting, reviewing, and approving the required documentation from the MTN 004 participating sites. Included in this step will be MTN CORE review of each site-specific study informed consent form prior to IRB submission.

This document provides an explanation of the regulatory background for this policy as well as definitions and procedures required for compliance. All sites participating in the MTN 004 study must comply with this policy.

6.2 Federal Regulations

All research funded by NIH must comply with Title 45 Part 46 of the Code of Federal Regulations (45 CFR 46) and the Food and Drug Administration (FDA) 21 CFR 50 (for IND studies).

These documents can be found at http://www.hhs.gov/ohrp.

The MTN 004 study must be reviewed by an appropriately constituted institutional review board (IRB) or Ethics Committee (EC) under a Federal-wide assurance (FWA). NICHD must have a record of this

review and approval through the ATN-DOC prior to implementation of the protocol. All amendments to the protocol, informed consents, or other study-related documents must be approved by the IRB/EC, and where necessary by Starpharma to the FDA, prior to implementing the amendment.

Information on registering an IRB and obtaining a FWA can also be found at http://www.hhs.gov/ohrp.

MTN-funded personnel with questions about general IRB issues should contact NICHD program staff.

6.3 Federal Regulations and Informed Consent

6.3.1 Basic Elements and Appropriate Additional Elements

Basic elements and appropriate additional elements as outlined in 45 CFR § 46.116 and 21 CFR § 50.25 include:

- Statement that the study involves research
- Purposes, duration, and procedures
- Foreseeable risks or discomforts
- Identification of any procedures which are experimental
- Reasonably expected benefits to subject or others
- Disclosure of alternative procedures
- Confidentiality measures
- Compensation, if any, for injury
- Contact people for the study
  - In case of injury
  - For research questions
  - Questions about rights
- Participation is voluntary

Additional elements that the IRB may require:

- Risks to fetus
- Circumstances under which participation may be terminated
- Additional costs to subject
- Consequences of the decision to withdraw

- New findings will be provided
- Approximate number of study subjects

6.3.2 MTN 004 Consent Form Templates

The MTN 004 protocol team has provided sample consent forms as appendixes to the MTN 004 study. These sample consent forms are reviewed by NICHD and approved as representing NICHD's assessment of the risk-benefit analysis of the study, and as providing accurate and understandable information to potential subjects and a sound portrayal of study requirements.

For sites that will recruit Spanish-speaking subjects and do not require their own local translations, the ATN-DOC will provide a certified translation of the consent form. This document must be approved by the site's IRB and submitted with registration documents. If the IRB makes changes, the ATN-DOC will request IRB approval of the Spanish consent (indicating that all required elements have been retained) and a letter certifying the translation.

6.3.3 Local Changes to MTN Consent Form Templates

If a site elects or is required by its IRB to delete or make any substantive change to the required elements in the protocol's sample consent, these changes must be highlighted and a written justification from the PI must be included in the registration packet. These changes must be shipped overnight to the ATN-DOC and will be shared with PAMAB/NICHD.

SUBSTANTIVE CHANGE DOES NOT INCLUDE FORMATTING ALTERATIONS TO BE CONSISTENT WITH LOCAL IRB PREFERENCE.

In addition, the minutes of the IRB meeting (or letter from the IRB) must reflect the justification for and the approval of the modifications to the aforementioned sections of the consent form. Consent forms must be the exact consents to be submitted to subjects. There must be no strikeouts in the Informed Consent document. The original IRB approved site consent(s) is to be kept on file at the site.

6.3.4 Subsequent Changes to Previously-Approved Consent Forms

The ATN-DOC must ensure that every consent form used in MTN 004 meets Federal requirements and presents accurate information. Further, the ATN-DOC must have the most current consent form on file. If changes are made to the IRB approved informed consent document **at any time,** the ATN-DOC must receive a copy of the revised IRB approved informed consent with changes highlighted. The ATN-DOC must review and approve the informed consent prior to a site using the document to obtain consent. Consent forms reviewed by the DOC must be the exact consents to be submitted to subjects.

6.4 Continuing Review

The ATN follows HHS regulations in Section 46.019(e), which requires that the IRB review research at intervals appropriate to the degree of risk, but not less than once per year. Sites are responsible for resubmitting their protocols, informed consents, and other supporting documentation to their IRB for continuing review. Once the IRB has approved the continuing research, the site should submit the following to the ATN-DOC:

- MTN 004 Registration Checklist (Exhibit ___)
- New approval from the IRB which includes:
  - Complete protocol title;
  - Protocol/study number and version number;
  - Date of IRB approval;
  - Signature of IRB Chairperson or member designee *;
  - Title of the person signing for the IRB;
  - Expiration data; and
  - Documentation of the IRB/EC designation of a risk/benefit category from 45 CFR 46.404-407.
- New approved consent forms

* Electronic IRB signatures are acceptable as long as the site provides to the DOC a one-time memorandum from the IRB that validates their electronic signature procedure.

If the new consent forms differ significantly from the template, follow the procedure in Sections 6.3.3 and 6.3.4, "Changes to Sample Consent Forms." Once the DOC receives these records, it will send an acknowledgement of receipt and approval or request for changes.

6.4.1 Sites *May Not* Enroll or See Patients Under a Protocol When IRB Approval has Expired

6.4.2 Sites *May Continue* to see Patients Under a Protocol if the IRB has Approved it but the DOC has Not Yet Confirmed Receipt

6.5 ATN Guidance Documents for Human Subjects Protections for Minors

Site staff preparing study protocol documents for the IRB should always adhere to the requests made in the protocol (e.g., waivers of parental permission or written consent forms). Conversely, no site staff should request a waiver if this waiver is not requested in the protocol itself. The protocol team may always be queried for guidance in these matters.

6.6 Designation of Risk/Benefit Category and Approval of Clinical Studies for Inclusion of Children by Institutional Review Boards/Ethics Committees

For research projects including children or adolescents, the National Institute for Child Health and

Human Development (NICHD) requires documentation of the IRB/EC designation of a risk/benefit category from 45 CFR 46.404-407 and IRB/EC approval for involvement of children based on the determinations specified in that category. The documentation may be in the IRB/EC approval letter or in other official correspondence from the IRB/EC to the investigator.

This documentation will be required to complete MTN protocol registration for all clinical studies enrolling children or adolescents that are reviewed by an IRB/EC. This requirement applies to the initial and annual IRB/EC reviews of research protocols and to any subsequent reviews of amendments or Letters of Amendment involving potential study risks or benefits. Protocol registration will not be approved if this documentation is not received.

Below are allowable risk/benefit categories for involving children and adolescents as subjects:

45 CFR §46.404 Risk not involving greater than minimal risk.

45 CFR §46.405 Research involving greater than minimal risk but presenting the prospects of direct benefit to the individual subjects.

45 CFR §46.406 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects but likely to yield generalizable knowledge about the subject's disorder or condition.

45 CFR §46.407 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health of welfare of children. (This category requires a special level of Department of Health and Human Services beyond that provided by the IRB/EC review. For further information, see http://www.hhs.gov/ohrp/children/guidance_407process.html May 26, 2005 guidance, "Children involved as subjects in research: Guidance on the HHS 45 CFR 49.407 review process."

6.7 Registration Process for MTN 004 Sites

Each site that intends to implement MTN 004 new or revised protocol must receive BOTH the approval of the IRB responsible for that site AND the approval of PAMAB/NICHD (through the ATN-DOC) before enrolling subjects in that study. In order to receive approval from the ATN-DOC for each version of the protocol, a site must ship overnight or fax all required documentation to the Regulatory Department of the ATN-DOC at the address listed at the end of Section 6.9. After these materials are submitted, the regulatory associate will follow up with the site if necessary to retrieve any missing information. Once these materials are complete and accurate, the ATN-DOC will notify the sites of approval to begin enrolling subjects within three business days.

6.7.1 New Protocol Versions

Once a new version of a protocol is distributed, sites may no longer register for a previous version of the protocol. Sites registered to participate in a previous version of the protocol are required to submit the current amended version to their IRB within 30 calendar days of distribution of the protocol to the sites. Subjects may be enrolled in the previous version for up to 90 days after the new version is distributed to the sites. Once the new

version is registered by the ATN-DOC for a site, all active subjects consented under the previous version must be re-consented under the new version. In general, and unless instructed otherwise, subjects will be re-consented at the next research visit after the protocol has been registered by the ATN-DOC.

6.8 Procedures for Protocol Registration

6.8.1 Required Documents

These documents are required for **each protocol and any subsequent version**. The MTN 004 site must keep the original set of protocol registration documents on file. The site must submit for itself and each administratively-distinct subsite **one copy** to the ATN-DOC of the following materials:

- MTN Protocol Registration Checklist (Exhibit __);
- Documentation of IRB approval (see section 6.8.2);
- IRB approved consent forms (see Section 6.3);
- Human Subjects Protection Monitoring Form (Exhibit __).
- A copy of Form FDA 1572
- Completed Clinical Investigator Financial Disclosure Form for each person on Form FDA 1572
- Institute Federal Wide Assurance Number (FWA)
- CV-signed and dated for site IoR
- HSP training certificates for all personnel listed on Form FDA 1572
-

6.8.2 Documentation of IRB Approval

IRB approval must include the following items:

- Complete protocol title;
- Protocol/study number and version number;
- Date of IRB approval;
- Signature of IRB Chairperson or member designee;
- Title of the person signing for the IRB;
- Expiration Date; and
- Documentation of the IRB/EC designation of a risk/benefit category from 45 CFR 46.404-407.

6.9 Exemptions

If a site cannot meet all the specific protocol registration requirements as outlined in Section 6.8 (due to IRB constraints, usual practice, or other restrictions), then a request for exemption, with relevant documentation, can be submitted to NICHD Program Staff through the ATN-DOC. These requests will be considered on a case by case basis. An example may include accepting an IRB's internal version numbering system on official IRB correspondence.

Send all registration materials to:

DOC Regulatory Associate: Aileen Kim
Westat
1441 West Montgomery Ave
Room WB 331
Rockville, MD 20850
Phone: 301-738-3642
Fax: 301-692-2149
Email: AileenKim@Westat.com or Regulatory@westat.com
Or

DOC Regulatory Manager: Marci Aderiye
Westat
1441 West Montgomery Avenue
Room WB 346
Rockville, MD 20850
Phone: 240-453-2645
Fax: 301-692-2149
Email: MarciAderiye@Westat.com or Regulatory@Westat.com

MTN Protocol Registration Checklist

SECTION I

Date of Submission: |___|___|–|___|___|–|___|___|___|___| Number of Pages ***(Including cover):*** |___|___|

This registration is for [Site Name]:_____

ATN Site Number:
|___|___|
Protocol Number: |___|___|___| Version Number: |___|___| Version Date:|___|___|–|___|___|–|___|___|___|___|

Investigator of Record ***(Please print):***_____

Phone Number: _____ E-mail Address: _____@_____

Name of Person Submitting Registration:_____

Phone Number: _____ E-mail Address: _____@_____

Name of Study Coordinator(s) who has/have completed protocol training:
(Please print)

_____ _____
_____ _____

Phone Number: E-mail Address: @

Site Pharmacist ***(Please print):***_____

Fax Number:_____ E-mail Address: _____@_____

Signature of Person Submitting Registration:_____

SECTION II *(Check the Type of Submission)*	**SECTION III** *(Required Documents)*	**EMAIL RESPONSE FROM ATN-DOC**
☐ Protocol Registration	MTN Protocol Registration Checklist plus materials in 6.8.1	Approval of Protocol Registration or Disapproval with request for changes.
☐ Corrected materials	As required by ATN-DOC	Approval if changes are complete and accurate.
☐ Annual IRB Renewal	MTN Protocol Registration Checklist, IRB Approval Letter, plus consent forms (if applicable)	Approval of IRB Renewal or Disapproval with request for changes.
☐ Deregistration/Study Closure	MTN Protocol Registration Checklist Documentation of IRB approval	ATN-DOC acknowledges closure (NO APPROVAL NEEDED)
☐ Other – Please explain _____	MTN Protocol Registration Checklist Documentation of IRB approval	Acknowledgment of receipt for all but Early Termination. (NO APPROVAL NEEDED UNLESS EARLY TERMINATION)

Human Subjects Protections Monitoring Form

Site Number: |___|___|___|___| Protocol/Study Number: |___|___|___|___| Version Number: |___|___|

Signature of Person Completing this Form: _____ Date: |___|___|-|___|___|-|___|___|___|___|

Please review the Protocol's Human Subjects Section and complete this form.

☐ Check here if this study requested no exemptions or waivers. ***(STOP)***

1. Did this study request an exemption as not constituting human subjects research? ☐ Yes ☐ No ***(Go to Q2)***

1a. Did you request this exemption from your IRB? ☐ Yes ***(Go to Q1b)*** ☐ No
If no, explain why not_____

_____

1b. Did your IRB grant the exemption? ☐ Yes ***(STOP)*** ☐ No
If no, explain why not_____

_____

2. Did this study request a waiver of written informed consent? ☐ Yes ☐ No ***(Go to Q3)***

2a. Did you request this waiver from your IRB? ☐ Yes ***(Go to Q2b)*** ☐ No
If no, explain why not_____

_____

2b. Did your IRB grant the waiver? ☐ Yes ***(Go to Q3)*** ☐ No
If no, explain why not_____

_____

3. Did this study request a waiver of parental permission for all youth age 12 and older? ☐ Yes ☐ No ***(Go to Q4)***

3a. Did you request this waiver from your IRB? ☐ Yes ***(Go to Q4)*** ☐ No
If no, explain why not_____

_____

3b. Did your IRB grant the waiver? ☐ Yes ***(Go to Q4)*** ☐ No
If no, explain why not_____

_____

4. Did this study request a waiver of parental permission conditional on specific criteria (e.g.,16 yrs or older, accessing care alone, and/or other criteria)? ☐ Yes ☐ No***(STOP)***

4a. Did you request this waiver from your IRB? ☐ Yes ***(STOP)*** ☐ No
If no, explain why not_____

_____

4b. Did your IRB grant the waiver? ☐ Yes ***(STOP)*** ☐ No
If no, explain why not_____

_____