Section 5. Study Procedures

5 Introduction

This section provides information on requirements for study procedures in MTN-039, including screening, enrollment and participant follow-up visits.

Note: The study product used in this study is an insert containing Tenofovir Alafenamide/Elvitegravir which will be administered rectally. For ease and consistency of reference, throughout this Manual, and in select implementation materials, the study product will be referred to as either the "rectal insert" or "study insert."

5.1 Visit Locations

Given the nature of study procedures required to be performed during MTN-039, all study procedures for screening, enrollment, dosing and the 24-, 48- and 72-hour post dosing visits should ideally occur at the study clinic. However, for all study visits, sites may utilize telephone or online applications to conduct appropriate visit procedures in a remote fashion in order to limit time spent in the clinic. This may include, but is not limited to, remotely conducting interviews, providing protocol counseling, and administering CASI surveys, when applicable. Any modifications to study visits will be documented accordingly in the study database. The final contact/Visit 11 (occurring approximately 3-7 days after Visit 10) may be conducted in-clinic or by phone.

5.2 Eligibility Determination SOP

It is the responsibility of the site Investigator of Record (IoR) and other designated staff to ensure that only participants who meet the study eligibility criteria be enrolled in the study. Each study site must establish a standard operating procedure (SOP) that describes how study staff will fulfill this responsibility. The SOP should contain, at a minimum, the following elements related to eligibility determination procedures, including:

- During-visit eligibility assessment procedures
- Post-screening visit eligibility assessment and confirmation procedures (i.e. review of laboratory results)
- Final confirmation and sign-off procedures prior to enrollment/randomization
- Documentation of each eligibility criterion (met or not met)
- Ethical and human subjects considerations
- Staff responsibilities for all of the above (direct and supervisory)
- QC/QA procedures (if not specified elsewhere)

5.3 Screening Visit

The term “screening” refers to all procedures undertaken to determine whether a potential participant is eligible to take part in MTN-039. The study eligibility criteria are listed in Protocol Sections 5.2 and 5.3; and required screening procedures are listed in Protocol Section 7.2.

5.3.1 Screening and Enrollment Timeframe

All protocol-specified screening and enrollment procedures must take place up to 45-days prior to enrollment/randomization. The 45-day window begins the day written informed consent is obtained (signed), even if no other procedures were done on that day.

Per protocol Section 7.2, multiple screening visits (as part of the same screening attempt) may be conducted if needed, to complete all required procedures. In cases where the screening visit is conducted over multiple days, all procedures are considered part of the same screening visit/screening attempt.

The term “screening attempt” is used to describe each time a participant screens for the study (i.e., each time they provide written informed consent for participation in the study). Potential participants may undergo one additional screening attempt, per the discretion of the IoR or designee.

If all screening and enrollment procedures are not completed up to 45 days of obtaining written informed consent, the participant must repeat the entire screening process, beginning with the informed consent process. This will be counted as the participant’s rescreen attempt. When rescreening participants, all screening procedures need to be repeated. Note, however, a new participant identification number (PTID) is not assigned to the participant in this case. Rather, the original PTID assigned at the first screening attempt is used for any repeat screening attempts, as well as future study visits should the participant successfully enroll in the study.

5.3.2 Screening Visit Procedures

Required screening procedures are specified in protocol section 7.2 and reflected in the applicable visit checklist available on the MTN-039 webpage.

After provision of written informed consent, participants will be assigned a PTID and undergo a series of clinical evaluations, laboratory tests and a behavioral eligibility assessment. Locator and demographic information will also be obtained. Participants will be reimbursed for their time and scheduled for enrollment, if found presumptively eligible.

Further details on PTID assignment, structure, and related information are included in SSP Section 12.

Behavioral eligibility criteria at screening, which are based on self-report, should be evaluated by administration of the Screening Behavioral Eligibility worksheet, provided on the MTN-039 webpage. It is suggested that staff administer this questionnaire early in the visit so that more time-consuming clinical and laboratory evaluations can be avoided if the participant is determined ineligible due to behavioral criteria (unless sites decide to administer clinical and laboratory evaluations regardless of eligibility as a service to the participant).

Clinical screening visit procedures, as described in detail in SSP Section 9 (Clinical Considerations), required for all participants are as follows:

- Collection of medical history, use of concomitant medications and evaluation of prohibited medications/products
- Conduct of a full physical exam to assess overall general health and a rectal exam to assess participants' baseline genital signs/symptoms
  - A male genital and pelvic exam may be conducted if clinically indicated
- Provision of all available test results and treatment or referrals for UTI/RTI/STIs

Details regarding laboratory tests and sample collection at screening are provided in SSP Section 11 (Laboratory Considerations). In summary, participants will receive testing for HIV 1/2, Hepatitis B surface antigen (HBsAg), STIs (GC/CT, Syphilis and if applicable, TV), coagulation (PT/INR), serum chemistries (creatinine, AST, ALT), CBC with platelets and differentials and pregnancy (if applicable).

Participants will also be counseled about HIV and receive appropriate pre- and post-test counseling as well as risk reduction counseling including the provision of condoms.

Protocol contraceptive requirements are only applicable to participants of child-bearing potential. For this reason, counseling on effective contraceptive use will be provided as applicable.

5.3.3 Screening and Enrollment Log

The DAIDS policy on Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials requires study sites to document screening and enrollment activity on screening and/or enrollment logs. A sample Screening and Enrollment Log suitable for use in MTN-039 is available on the MTN-039 Study Implementation Materials webpage. Study sites are encouraged to reference the eligibility codes listed at the bottom of the sample log when recording the reason(s) for screening failure/discontinuation.

5.3.4 Participants Found to be Ineligible (Screen Failures)

Screening procedures should be discontinued when the participant is determined to be ineligible. For all participants who screen fail, the following should be in place:

- Completed ICF(s)
- Reason(s) for ineligibility, with date of determination, documented in chart notes and on the Inclusion Exclusion Criteria CRF
- If a participant screens out due to a clinical condition requiring follow-up, appropriate referrals should be provided to ensure well-being of the participant and documentation of all referrals should be included in the participant chart.
- Necessary referrals on file (as appropriate) and documentation that any clinically significant abnormalities (labs, etc.) were provided and explained to the participant within a reasonable timeframe (even if referral is not necessary), regardless of eligibility determination.
- All source documentation completed up until the time that ineligibility was determined
- Chart notes complete up until the time ineligibility was determined
- Indication of what visit procedures were conducted on the visit checklist
- Complete row on the Screening and Enrollment Log, updated with date of discontinuation of screening and reason for screen failure.

5.4 Enrollment Visit

The participant's final eligibility status should be determined by evaluating and then marking off all items on the MTN-039 Eligibility Checklist. The Eligibility Checklist should be completed on the day of enrollment and the site IoR (or designee) and a second staff member should sign and date the Eligibility Checklist to confirm and verify eligibility status prior to randomizing the participant. If the participant is

found ineligible before the enrollment visit, the Eligibility Checklist does not need to be completed. If a participant is found to be ineligible during the enrollment visit and the checklist has been partially completed, there is no need to continue filling out the checklist past the point when ineligibility is determined.

A participant is considered enrolled in the study only after they have been randomly assigned to a sample collection sequence.

Further information on methods and materials for sampling assignment is provided in the SSP Section 12 (Data Collection).

Should site staff identify that an ineligible participant has inadvertently been enrolled in the study, the IoR or designee should contact the MTN-039 Protocol Safety Review Team (PSRT) and the MTN-039 Management Team for guidance on subsequent action to be taken.

5.4.1 Enrollment Visit Procedures

The Enrollment Visit serves as the baseline visit for MTN-039. All procedures for this visit must be conducted on the same day and cannot be split across multiple days.

Study enrollment procedures are specified in protocol section 7.3 and reflected in the Enrollment Visit Checklist (available on the MTN-039 webpage). The following procedures will be completed as part of eligibility confirmation prior to randomization on the day of enrollment.

The following procedures will be conducted:

- Review and update locator information
- Review informed consent and confirm participant remains interested in continued study participation
- Confirm behavioral eligibility criteria (through administration of the Enrollment Behavioral Eligibility Worksheet)
- Review and update medical and concomitant medications history since screening visit. Evaluate use of prohibited medications, STI/UTIs, genital or reproductive track signs/symptoms, and overall general health.
- Provide contraceptive counseling to those of child-bearing potential
- Collect urine to test for pregnancy (for those of child-bearing potential) and if clinically indicated, conduct a dipstick UA and/or urine culture for all participants
- Collect blood for: PK, HIV-1/2 testing and plasma archive. If indicated, collect blood for serum chemistries, CBC with differential and platelets and syphilis serology.
- In conjunction with HIV testing, provide HIV pre- and post-test counseling as well as HIV/STI risk reduction counseling and offer condoms.
- Conduct a full physical exam to assess overall general health.
- Conduct a rectal (and if indicated, male genital and pelvic) exam(s) to confirm eligibility and collect baseline anorectal and pelvic samples, and test for STIs, if indicated.
- Participants should receive all available test results and treatment or referrals for STI/UTIs and reproductive tract infections.
- Provide protocol adherence counseling. Note: This may also be conducted after randomization, but it could be helpful to provide the participant with more information about the study product prior to their final decision to enroll in the study.
- Once it is clear that the participant is likely eligible, complete the Baseline CASI questionnaire.

Once the above-mentioned procedures and final determination of participant eligibility have been completed by designated site staff, the participant may be randomized to a study sample collection

sequence, at which point they will be considered officially enrolled in the study. See SSP Section 12 (Data Collection) for information on completing the randomization process.

After randomization, the following procedures will be conducted:

- Disclose and explain the participant's study sample collection sequence assignment
- Provide site contact information, condoms, and any other study instructions
- Provide and explain enema kit to be administered at home prior to the scheduled dosing visit, along with preparation and administration instructions
- Provide reimbursement
- Update participant's study visit calendar and schedule next visit (to occur at least 7 days after enrollment).

5.4.2 Pharmacokinetics, Pharmacodynamics, and Biomarker Sample Collection

On the day of Enrollment, participants will be assigned to one of two groups that will determine when genital samples (rectal fluid and tissue; and if applicable, vaginal fluid) will be provided on the day of and following product administration. Once a participant has received a timepoint assignment at Enrollment, that same assignment is maintained across each dosing regimen. Refer to protocol section 7.10 and the applicable Genital Exam checklist for required sampling timepoints for Groups 1 and 2. In brief:

At Dosing Visits (3 and 7):
Rectal and vaginal samples will be collected as follows:

- Participants in both groups will be given a saline enema in clinic on the day of dosing at least 45 minutes prior to dose administration.
- Group 1 will have rectal (and if applicable, vaginal) fluid for PK collected at 2 and 6 hours post dose. Rectal (and if applicable, vaginal) fluid for PD and biopsies (for PK, PD and biomarkers) will be collected at 2 hours post-dose (window 1.5-2.5 hours).
- Group 2 will have rectal (and if applicable, vaginal) fluid collected 4-hours post dose (window 3.5-4.5 hours).
- Both groups will have blood for PK testing collected at hours 1, 2, 4 and 6 after the insert is administered. Clinicians should aim to start the blood draw exactly at the targeted collection time (i.e., on the hour). Minor excursions from the target collection times may occur but should be no more than +/- 15 minutes.

At 24-hour Post Dosing Visits (4 and 8):

- Efforts should be made to collect samples 24 hours following product administration. However, a +/- 2-hour window permitted allowing the visit to be conducted between 22 and 26 hours after each dosing visit.
- Those assigned to Group 2 will provide rectal tissue, rectal fluid and, if applicable, vaginal fluid.
- Both groups will have blood for PK testing collected.

At 48-hour Post Dosing Visits (5 and 9):

- Efforts should be made to collect samples 48 hours following product administration. However, a +/- 4-hour window is permitted allowing the visit to be conducted between 44 and 52 hours after each dosing visit.
- Those assigned to Group 1 will provide rectal tissue, rectal fluid and, if applicable, vaginal fluid. These participants will have a rectal saline enema performed in the clinic after swab collection but prior to the rectal biopsy and sigmoidoscopy procedures.
- Both groups will have blood for PK testing collected.

At 72-hour Post Dosing Visits (6 and 10):

- Efforts should be made to collect samples 72 hours following product administration. However, a +/- 6 hour window is permitted allowing the visit to be conducted between 66 and 78 hours after each dosing visit.

- Those assigned to Group 2 will provide rectal tissue, rectal fluid and, if applicable, vaginal fluid. These participants will have a rectal saline enema performed in the clinic after swab collection but prior to the rectal biopsy and sigmoidoscopy procedures.
- Both groups will have blood for PK testing collected.

At the Dosing visits, the rectal exams should be done prior to insert administration to ensure there is no clinical indication to defer dose administration. The rectal and pelvic samples should be taken as required after dose administration. At the 24-, 48- and 72-hour visits, rectal and pelvic samples should be collected while conducting the rectal examination.

Table 5-1 below shows the time-point sequence and applicable windows for samples collected post dose administration.

Table 5-1: Sample Collection Time-Points Post-Insert Administration

Study Visit	**Blood Samples** (All time-points required for all participants)	**Rectal/Pelvic Samples** (per sample collection sequence assignment)
Enrollment	1 time during visit (no specified time; no dose administration)	1 time during visit (no specified time; no dose administration)
Dosing Visit (V3 and 7)	1 hours 2 hours 4 hours 6 hours (+/- 15-minute window permitted for hourly times)	Group 1: 2 and 6 hours, when applicable Group 2: 4 hours (+/-30-minute window permitted)
24-Hr Post-Dose Visit (V4 and 8)	24 hours (+/- 2 hours window permitted)	Group 2 only (+/- 2 hours window permitted)
48-Hr Post-Dose Visit (V5 and 9)	48 hours (+/- 4 hours window permitted)	Group 1 only (+/- 4 hours window permitted)
72-Hr Post-Dose Visit (V6 and 10)	72 hours (+/- 6 hours window permitted)	Group 2 only (+/- 6 hours window permitted)

Sample collection must begin and be completed within the specified time periods. Any excursions that occur (e.g. the final sample is collected after the window closes) should be documented as protocol deviations.

5.5 Follow-up Visits

Throughout the study follow-up period, two types of follow-up visits may be conducted (interim and scheduled visits).

Scheduled visits are those visits required per protocol. Each participant will complete a total of eight clinic follow-up visits, followed by the final contact/termination visit.

- Dosing Visits (Visits 3 and 7): Visits at which the EVG/TAF insert(s) is administered
- 24-Hour Post-Dosing Visits (Visits 4 and 8)
- 48-Hour Post-Dosing Visit (Visits 5 and 9)
- 72-Hour Post Dosing Visits (Visits 6 and 10)

- Visit 11 (Follow-up Contact/Termination): This contact could be either an in-clinic visit or a telephone contact.

All participants will have a washout period between each dosing visit. **The washout period must be a minimum of 1 week (7 days) and a maximum of 7 weeks (49 days).** The washout period should be timed to occur at least 7 days after the participant's last tissue sampling visit (i.e. Visit 5 for Group 1 or Visit 6 for Group 2) and if applicable, should coincide with female participants' menses as to avoid vaginal bleeding during dosing and post-dosing visits.

Interim visits are those visits that take place between scheduled visits. These visits may be performed at any time during the study, and any visit procedures may be conducted as indicated. All interim contacts (e.g., phone calls and/or clinic visits) will be properly documented in study files and on applicable CRFs. Procedures required during an interim visit will depend on the reason for the visit. For example, if a participant presents to the site to report an AE, all clinically-related procedures to assess the AE and required documentation would be the required procedures for that interim visit. See SSP Section 12 (Data Collection) for more details on recording interim visits.

In accordance with LoA #03, if there is a gap of ≥60 days between visits for a participant, the participant will be asked to return for an interim visit for additional safety evaluation prior to the next scheduled visit to confirm the absence of any clinical symptoms, recent illness, or acquisition of HIV or STIs.

5.5.1 Visit Windows

Acknowledging that it will not always be possible to complete follow-up visits on the targeted dates, the MTN-039 protocol allows for certain visits to be completed within a visit window, if possible. A complete listing of visit windows is available in SSP Section 12 (Data Collection).

Sites are encouraged to complete required study visits on the target day, if possible. If this is not possible, the visit may be completed within the visit window (for visits with a window). Visits completed within the visit window will be considered completed ("retained") visits.

Although the visit windows allow for some flexibility, the intent of the protocol-specified visit schedule is to conduct follow-up visits at specific intervals. A visit scheduling tool is available on the MTN-039 webpage that can be used to create follow-up visit schedules for enrolled participants.

5.5.1.1 Visits Conducted Over Multiple Days: "Split Visits"

All procedures specified by the protocol to be performed at a follow-up visit, ideally, will be completed at a single visit on a single day. If all required procedures cannot be completed on a single day (e.g., because the participant must leave the study site before all required procedures are performed), the remaining procedures may be completed on subsequent day(s) within the allowable visit window, if that visit has a window. When this occurs, the visit is considered a split visit. As described in SSP Section 12 (Data Collection), all CRFs completed for a split visit are assigned the same visit code (even though the dates recorded on the CRFs may be different).

If study visits must be split, please ensure that:
- HIV pre-test counseling and HIV testing occur on one day (note: if HIV testing is done using a rapid test, posttest counseling should also occur on the same day).
- PK/PD/Biomarker specimens are collected on the same day to avoid complicating interpretability of the data.

Any procedures that are not conducted within the visit window will be considered missed. See section 5.5.1.2 below for guidance on which missed procedures should be made up at an interim visit.

5.5.1.2 Missed Visits

For participants who do not complete any part of a scheduled visit within the allowable visit window, the visit is considered "missed," and a Missed Visit CRF must be completed to document the missed visit (see the CRF completion guidelines for more information on completion of this form).

Given the wide washout period (1-7 weeks) between doses, it is unlikely that a dosing visit (V 3 or 7) will be missed. To avoid missed dosing visits, participants should be scheduled early enough in the visit window to allow for rescheduling within the window, if needed. Otherwise, if a participant misses a dosing visit, they will be permanently discontinued from study product and exited from the study.

If a Post-Dosing visit is missed after the participant receives their dose, sites must make every effort to make up the missed visit and required study procedures (as soon as possible and ideally within 3 days of dose administration) at an interim visit and retain the participant for their remaining scheduled study follow-up visits.

In any of these missed visit scenarios, sites should contact the MTN-039 Management Team for additional guidance.

5.5.2 Follow-up Visit Procedures

Required follow-up visit procedures are listed in protocol section 7.4. Several additional clarifications of the procedural specifications are provided in the remainder of this section. While sites should aim to perform procedures in the order indicated on their site-specific visit checklists, this might not always be possible. Further operational guidance on completing protocol-specific procedures, including procedure order during follow-up, is incorporated into the sample visit checklists and in SSP Section 2 (Documentation Requirements).

As a general guide, during follow-up, the following will occur in addition to the PK/PD/Biomarker sample collection schedule noted in section 5.4.2 above:

- Locator information must be obtained/reviewed at every visit.
- Protocol counseling will be provided at all visits, with the exception of the final contact. This may be customized to individual participant needs and abbreviated as applicable.
- Medical and medication histories interim review, AE assessment and documentation, assessment of concomitant medications and provision of any available lab results will be done at all visits.
- Rectal examination is conducted at every in-clinic visit; pelvic and male genital exams are done only as indicated at every visit.
- Provision of home saline enema kit at Visit 6.
- In-clinic insert administration occurs at Visits 3 and 7.
- Behavioral assessments via CASI are completed at the 24-hour post dosing visit (Visits 4 and 8) and the IDI is conducted at visit 10.
- Participants will be reimbursed for their time at each visit and scheduled for their next visit as applicable.
- Condoms will be offered at all visits, with the exception of the final contact, at which they will be offered if indicated.
- For females, a pregnancy test is and if clinically indicated at all other visits.
- HIV testing and counseling is required at Visit 10, and when clinically indicated.
- Chemistries (AST, ALT, creatinine) and CBC with differentials and platelets are required at Visit 10, and when clinically indicated.

5.5.3 Final Contact/ Termination Considerations

The Final Contact/Termination visit (Visit 11) may be scheduled as an in-clinic visit or as a phone call. At the preceding visit, site staff should discuss with the participant what procedures will be conducted during this final visit/contact and ensure the participant is agreeable and understands what may be expected after study termination.

After completing their final contact/termination visit, participants will no longer have routine access to services provided through the study, such as HIV counseling and testing. Participants should be counseled about this — ideally before and during their Final Contact/Termination visit — and provided information on where they can access such services after study exit. It is recommended that all study sites develop written referral sheets that can be given to participants; if the Final Contact/Termination visit is planned as a phone call, this information should be provided to the participant prior to study exit. If the Final Contact/Termination visit is planned as an in-clinic visit, this information could be provided to participants at that time.

Additional contacts after study exit may be required for:

- Participants who are pregnant during the study to obtain pregnancy outcome
- Participants with positive or indeterminate HIV rapid or confirmatory test results
  Participants with certain types of AEs that are ongoing at study exit

For each participant, any additional contact(s) should be scheduled based on the participant's overall clinical picture at study exit, as well as the time required to obtain all final study test results. It is recommended that follow-up contact plans be documented on chart notes or a site-specific tool (e.g. worksheet). All additional contacts must be documented in participant study records, but no CRFs are completed for these contacts.

All participants will be contacted post-study to be informed of the study results. Participant preferences for methods to be used for contacting them when study results are available should be documented in participant study records.

Lastly, for participants that study staff may wish to contact regarding participation in future studies, permission for such contact should be sought from the participant and documented. It is recommended that participant permission (or lack thereof) for future studies be documented on a study exit worksheet or other site-specific documentation that can be easily accessed by study staff.

5.5.4 Participants Who Become Infected with HIV

Study product should be temporarily held upon first reactive/positive HIV test. Study product use must be discontinued immediately for participants who are confirmed to be positive for HIV-1/2.

If a participant becomes infected with HIV-1/2 after the Enrollment Visit, they will be referred to local care and treatment services and may return to the clinic for additional counseling and other support services, as needed per site SOP.

Once HIV status is confirmed, study follow-up visits will be discontinued, and the participant will be considered terminated from the study. Participants who seroconvert after randomization may be offered additional laboratory testing (such as HIV RNA and HIV drug resistance testing).

5.5.5 Participants Who Become Pregnant

If a participant becomes pregnant, follow-up visits and procedures will be discontinued, and the participant will be considered terminated from the study (see protocol section 7.5.2). Participant will be referred to local health care services and may return to the clinic for additional counseling, as needed per site SOP.

Sites should develop a plan with such participants to attain the pregnancy outcome. One contact to obtain this information is sufficient. For example, the participant could call or e-mail the site to inform the site of the outcome.

5.5.6 Participants Who Permanently Discontinue Study Product for Other Reasons

For participants who permanently discontinue study product use for any clinician-initiated reason (other than HIV seroconversion or pregnancy) or for any participant-initiated reason (e.g., participant declines study product use or decides to withdraw from the study), the site IoR/designee may opt to discontinue study follow-up visits and procedures, after consulting the MTN-039 PSRT and Management Team. If a participant permanently discontinues study product use due to an AE, the site must continue to follow the participant until resolution (return to baseline) or stabilization of the AE is documented.

If study participation is discontinued, participants will be asked to complete an early termination visit, if willing.

If follow-up continues, participants will continue to come in for protocol-specified follow up visits through their scheduled termination/final contact.

5.5.7 Criteria for Early Termination of Study Participants

As outlined in Protocol Section 9.6, participants may voluntarily withdraw from the study for any reason at any time. The IoR/designee also may withdraw participants from the study to protect their safety and/or if they are unwilling or unable to comply with required study procedures, after consultation with the PSRT. Participants also may be withdrawn if CONRAD; NIAID; the MTN; government or regulatory authorities, including the FDA and Office for Human Research Protections (OHRP); or a site IRB/EC terminate the study prior to its planned end date.

The Final Contact/Early Termination Checklist should be used as a guide for early termination procedures, if the participant is willing to complete one last visit. If the participant is terminating early from the study for any reason, staff should complete the following:

- Record the reason(s) for the withdrawal in participants' study records.
- Consult the PSRT regarding early terminations per IoR decision and print and file outcome correspondence in the participant chart. PSRT consultation is not required for voluntary withdrawals.
- Update participant locator form, and document how the participant would like to receive any follow up test results (as needed) and be informed of study results.

5.5.8 Replacing Participants

Additional participants may enroll in the study, per protocol section 10.4, at the discretion of the Protocol Team, to replace currently enrolled participants lost to follow-up or to permanent product discontinuation. Replacement decisions will be made on a case-by-case basis by the MTN-039 Management Team. If a site believes a participant may need to be replaced, the site should email the Management Team and provide the following information: PTID, date of enrollment, current follow-up status (i.e. where the participant currently is in their visit schedule), reason for replacement request, whether product administration occurred as intended and date of next scheduled enrollment.