1. Documenting and Recording Protocol Deviations

Subject Related Protocol Deviations:

- Should be recorded in the visit notes in the medical records or documented on the Protocol Deviation Source Worksheet.
    - If utilizing the source worksheet, capture one deviation per form.
- Deviation-related source documents should be filed in the subject binder, as applicable.
- Enter deviation(s) into the EDC System.

2. Reporting Protocol Deviations – Site Responsibility

2.1 How do I Report Protocol Deviations to the Sponsor?

- Should a protocol deviation occur during the study, Site should report the protocol deviation to the following:

  eCRF in EDC (Medidata)

  IRB, if applicable

    - Please refer to both your site's IRB Guidelines and your site's SOPs for reporting protocol deviations.
    - If uncertain, please discuss with the IRB and Sponsor.

3. Common Protocol Deviations

Protocol Deviation	Recommendation to Avoid Future Deviations
Follow-Up Visit: • Completed before or after window • Missed entirely	• Work with your site manager to review scheduled visits. • Try to schedule visits at the beginning of the follow-up window. In the event subject calls to reschedule or misses the visit, this will give time to reschedule a new visit within window.
Assessments and Laboratory Tests: • Completed before or after window • Not Done	• Review the testing required for that visit. If a clinic nurse or separate lab is performing the test, ensure they are aware of the requirements.
Study Assessments • Completed before or after window • Not Done	• Make every attempt to perform study assessments in window via an in-office visit or by phone as required. • If for some reason an office visit is required but not possible, proceed with a telehealth or phone visit.
Subject Informed Consent: • Not collected/documented appropriately	• Review signed ICF prior to performing study-specific procedures. • Ensure the most current ICF version clearly labeled and available.

	• If your IRB requires initials/dates on each page, review each page to ensure completed
<u>Study Medications</u> • Dose changed or stopped sooner than 6 months post-procedure, per protocol	• Document reason for medication deviation and store source documentation in patient binder.
<u>Adverse Event (AE) Reporting</u>	• **AE:** Enter in EDC (and optionally, complete source worksheet) as soon as possible, but no later than 10 working days from the date of awareness. ○ Note: adverse event source should be signed off by PI. • **SAE:** Notify Sponsor within 2 working days in EDC • **UADE:** Notify Sponsor within 2 working days in EDC

4. Deviation from Protocol Deemed Necessary by PI

- PIs may deem a deviation from the protocol to be necessary to protect the safety and/or physical well-being of a subject.
- PI is requested to notify Sponsor as soon as possible and IRB/REB if required.
- This deviation is still required to be reported through the EDC