North Texas Regional Institutional Review Board

Guidance and Procedures for Investigators Topic:

Reporting Protocol Violations and Deviations

What are Protocol Violations and Deviations?

Protocol deviations are considered to be any change or departure from the IRB-approved study design, study procedures, or study materials of a research project. In some instances, these deviations may affect the rights, safety, or well-being of the subject(s); the risk/benefit ratio of the study; and/or the completeness, accuracy, or reliability of the collected study data.

In many cases, protocol deviations that will also be defined as violations will fall into one of the following 5 categories:

1. The deviation has harmed, or posed a significant or substantive risk of harm, to the research subject.
2. The deviation has compromised the scientific integrity of the data collected for the study.
3. The deviation is a willful or knowing breach on the part of the investigator(s) of human subject protection regulations, institutional polices, or NTR IRB procedures.
4. The deviation involves serious or continuing noncompliance with federal, state, local, or human subject protection regulations, polices or procedures.
5. The deviation is inconsistent with the Human Research Protection Program's (HRPP's) / NTR IRB's research, medical, or ethical principles.

The following are examples of protocol deviations (this list is not intended to be exhaustive). Note that any of these deviations is also a protocol violation:

- Variations or errors in drug dosing/dispensing/storage, or in implementing the research intervention
- Use of prohibited medications
- Enrolling subjects who did not meet the inclusion/exclusion criteria
- Research subject met withdrawal criteria during the study but was not withdrawn
- Unauthorized (not IRB approved) persons (faculty, staff, students, residents, etc.) participating in the conduct of a research study
- Premature "unblinding" of research treatment or data
- Loss or corruption of collected subject samples and/or data
- Failure to obtain informed consent from a subject (or subjects) prior to initiation of study-related procedures

- Use of an unapproved or expired consent document or oral consent procedure
- Incorrectly performed or missing protocol-required tests and procedures
- Incorrect handling of biological samples
- Changing the protocol without prior IRB approval
- Falsifying research or medical records (note that this is also considered to be *research misconduct*)
- Performing tests or procedures beyond the professional scope or privilege status (credentialing)
- Unapproved persons accessing subjects' collected data, i.e., a breach in confidentiality
- Inadequate or improper informed consent procedures
- Failure to submit Data Safety Monitoring Board (DSMB) reports to the IRB in a timely manner (please see the NTR IRB SOPs for further information).
- Failure to report unanticipated problems involving risks to subjects or others, and adverse events (serious and/or unexpected) in a timely manner (please see the NTR IRB SOPs for further information)
- Protocol deviations/violations identified by sponsor monitor visits or the study coordinator that may affect the safety of the participant(s) or the integrity of the study data

Protocol violations should be reported to the North Texas Regional IRB within **10 working days** of discovery. This report must use the appropriate procedures described below.

Reporting of Errors that Occur During the Informed Consent Process

Examples of informed consent errors that may constitute a protocol violation include the following:

- Subject undergoes study procedure(s) prior to giving informed consent
- Subject signs an outdated or incorrect version of the consent form
- Subject undergoing research intervention is not re-consented when new information is incorporated into the consent form
- Other consenting error the study sponsor requires be reported to the IRB (if applicable).

Errors that occur during the informed consent process must be reported to the IRB within **10 working days** of discovery using the appropriate procedures described below.

What to Submit to the North Texas Regional IRB:

All reports of protocol deviations/violations must be submitted in the electronic submission system (in a new study package) to the IRB within **10 working days** of discovery.

The easiest way to provide all the necessary information to the IRB is by completing and submitting the Protocol Deviation / Violation Form located on the NTR IRB Forms webpage: https://www.unthsc.edu/north-texas-regional-irb/institutional-review-board-forms/ .

The IRB will also accept a memo/letter, signed by the Principal Investigator, which contains the following information (please note that the following information pertains to *ALL* studies, including funded or un-funded and clinical trials or investigator-initiated):

- IRB Project #, Subject ID #, Date(s) of the Event(s)
- Date study staff identified the event(s)/violation(s)
- Description of the protocol violation, including the cause of the event(s)
- How the event deviated from the protocol
- Investigator's assessment regarding any impact on risks to study participants resulting from the violation(s), as well as the PI's justification for this risk assessment. Include a description of additional treatment the subject required as a result of the violation (if applicable).
- Corrective action plan(s) that will be implemented to address the current violation(s) and to prevent similar violations from occurring in the future
- Date the study sponsor was notified of the violation (if applicable)

**If applicable, please also submit any relevant supporting documentation as separate attachments in the electronic submission system. This could include, but is not limited to, reports to the study sponsor regarding the violation(s); examples of unapproved documents used by the study team; lists of unapproved data variables that were collected by the study team; and so on.*

Please Note:

- ✓ ***Submission of the above form and/or memo does not preclude additional investigation or inquiry by IRB staff or the IRB.***
- ✓ ***Recurring non- compliance is reportable to federal agencies.***

Protocol Deviations - For Sponsored Clinical Trials:

Protocol deviations are considered to be those changes or alterations in the conduct of the study which do **not** have an impact on the subject's rights, safety, or well-being or

completeness, accuracy, or reliability of the study data. The following are examples of protocol deviations:

- A minor variation in clinic visits/follow up (e.g. "Day 10 visit" on day 14) if no protocol medication, treatment, or supervision is missed
- Collection of study data (e.g. temperature reading) performed incorrectly by subject or subject's parent/guardian
- Withdrawal of subjects for logistical reasons (e.g. moved out of town)
- Lab tests or study visit not being conducted at the correct time or date, but inside an acceptable time frame as defined by the study sponsor.

The IRB does not require that minor protocol deviations be reported by the investigator. However, if the study sponsor requires that the deviation be reported to the IRB, the IRB will provide acknowledgement of receipt and review of the deviation. In any case, investigators should always contact the IRB staff for guidance in determining if a deviation should be reported to the NTR IRB if they are unsure.

Guidance for Avoiding Protocol Violations

The Principal Investigator is the responsible party and will be held accountable for the conduct of the study. There are some steps that investigators can take to prevent or reduce the likelihood of protocol deviations or violations occurring during the conduct of their study. Here are several recommendations:

- It is important for all study personnel to be familiar with the protocol and understand their role in the study. The Principal Investigator should make sure that the delegation of tasks is well understood by the study personnel.
- Researchers should plan that protocol violations might occur during the study and have an agreed upon procedure for discussing and reporting them. For example, it is important to understand what type of documentation will be required by the sponsor, to determine who will notify the IRB of a violation, and to identify who will determine what course of action might be taken to prevent common protocol violations.
- Prepare study amendments in a timely manner and submit them to the IRB for review and approval before implementing the changes.
- Ensure that Serious Adverse Event (SAE) and DSMB reports are submitted to the IRB in a timely manner.
- Ensure that all key personnel working on a study are approved by the IRB to do so before beginning work on the study.
- Ensure that the investigator and the research team know the regulations pertaining to research with human subjects, as well as protocol violations.

For further guidance/questions regarding Protocol Violations, please reach out to the NTR IRB office at NorthTexRegIRB@unthsc.edu.