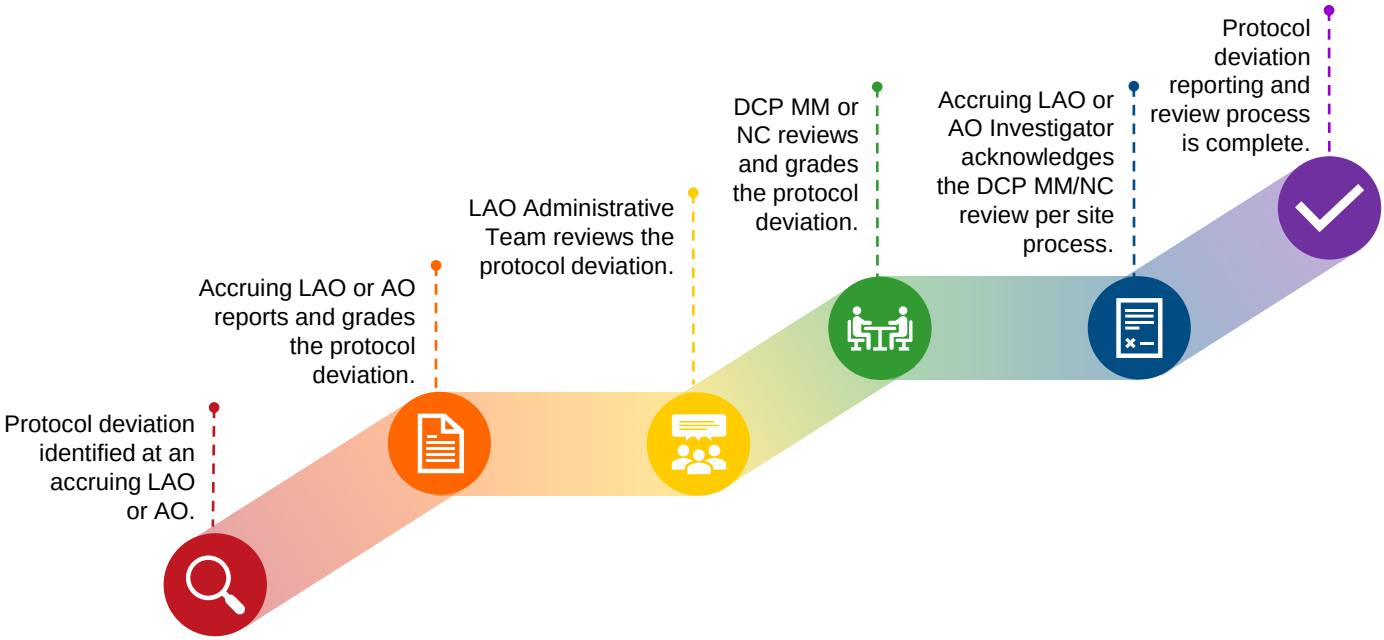
CP-CTNet QKREFGD17 *Grading CP-CTNet Protocol Deviations*

Protocol Deviation Reporting and Review Process Overview

A Cancer Prevention Clinical Trials Network (CP-CTNet) protocol deviation is any noncompliance with the study design and/or procedures of a Division of Cancer Prevention (DCP)-approved and Central Institutional Review Board (CIRB)-approved protocol. Protocol deviations may result from the actions of a participant, investigator, or clinical staff at the accruing Lead Academic Organization (LAO) or Affiliated Organization (AO). Investigators, coordinators, and LAO and AO designees are responsible for reporting protocol deviations as soon as they are identified at their accruing LAO or AO. Protocol deviations are reviewed by the LAO Administrative Team and the DCP Medical Monitor (MM) or Nurse Consultant (NC). See SOP 02-02 *Reporting Protocol Deviations* for more information. This section highlights the CP-CTNet protocol deviation reporting and review process.



Protocol Deviation Grade Overview

CP-CTNet protocol deviations are graded at two points during the reporting and review process. The accruing LAO or AO assigns an initial grade when they report a protocol deviation that occurred at their accruing LAO or AO. They are responsible for selecting between *minor* and *moderate/major* protocol deviation grades, which helps facilitate the timing of the DCP MM or NC review. The DCP MM or NC assigns a final grade (*minor, moderate,* or *major*) during their review of the protocol deviation. This section highlights the definitions of the three grades that accruing LAOs, AOs, DCP MMs, and DCP NCs use to grade CP-CTNet protocol deviations.

	Definition	Grade
Major	Protocol deviation will affect the integrity or reliability of research data or will affect participant rights or safety. • This includes all deviations related to inclusion/exclusion criteria, deviations related to data necessary for primary endpoints, and data necessary for key secondary endpoints.	3
Moderate	Protocol deviation has the potential to affect the integrity or reliability of research data or poses potential risk to participant rights or safety.	2
Minor	Protocol deviation has no meaningful effect on integrity or reliability of research data and no meaningful risk to participant rights or safety.	1

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The Importance of Accurately Grading Protocol Deviations

Although each protocol deviation receives a final grade from the DCP MM or NC, it is important for accruing LAOs and AOs to accurately grade protocol deviations during the initial protocol deviation reporting process. This section highlights four key reasons why grading protocol deviations accurately is important on CP-CTNet studies.

1

- The grade assigned by the accruing LAO or AO is used to determine the timing of the DCP MM or NC review:
  - **Minor**: Reviewed monthly.
  - **Moderate/Major**: Reviewed immediately after the LAO Administrative Team review.

2

- Accurately grading protocol deviations may provide the accruing LAO or AO with an increased understanding of the level of corrective action needed to address any safety or ethical concerns associated with the protocol deviation.

3

- Accurately grading protocol deviations may provide the LAO Administrative Team with valuable information about the severity of a protocol deviation trend occurring at an accruing LAO or AO, or across the entire study, so that they may appropriately address the trend.

4

- Accurately grading protocol deviations may provide statisticians with increased context when analyzing data for primary study endpoints and key secondary study endpoints at the end of the study.

Creating a Study-Specific Protocol Deviation Grade Checklist

Accruing LAOs and AOs can create a brief study-specific protocol deviation grade checklist to help facilitate the grading process. This informal checklist is intended to help accruing LAOs and AOs gather and evaluate the information necessary to assign an initial protocol deviation grade (*minor* vs. *moderate/major*). This checklist may also help guide study team discussions about protocol deviations and grade them in an objective way. This section provides brief steps that accruing LAOs and AOs can follow to create a study-specific protocol deviation grade checklist for the CP-CTNet studies that they participate in. The next section of this quick reference guide includes a blank sample study-specific protocol deviation grade checklist that accruing LAOs and AOs can use to organize the information needed to appropriately grade a protocol deviation that occurs on a CP-CTNet study.

1. Gather Study Information

- What are the primary study endpoints for this study?
- What are the key secondary study endpoints for this study?
- What are the risks to participant safety for this study?
- What are the ethical risks for this study?

2. Gather Event Information

- What happened in this situation?
- What part of the protocol does this event deviate from?

3. Create a Brief Checklist

- Add a row for each study endpoint, safety risk, and ethical risk identified in Step 1.
- Add three columns next to each listed item (e.g., *Yes, No,* and *Possibly*).
- Complete the checklist by indicating the impact of the protocol deviation on each item.

4. Assign the Grade

- If all answers are *No*, then grade the protocol deviation as **Minor**.
- If any answers are *Yes* or *Possibly*, then grade the protocol deviation as **Moderate/ Major**.

Blank Study-Specific Protocol Deviation Grade Checklist

Completion Instructions: Add questions for each of the primary study endpoints, key secondary study endpoints, participant safety risks, and ethical risks for the study beneath the *Study-Related Information* column. Then, place a checkmark in the appropriate *Yes*, *No*, or *Possibly* column in each row to assess the impact of the protocol deviation on each study endpoint or risk. Sample study-related questions may include:

- Does this protocol deviation impact the integrity or reliability of research data for (primary study endpoint 1)?
- Does this protocol deviation impact the integrity or reliability of research data for (key secondary study endpoint 2)?
- Does this protocol deviation impact the rights of the participant or any ethical safeguards that are outlined in (protocol section number)?
- Does this protocol deviation impact the participant's safety or well-being?

Study-Related Information	Yes	No	Possibly

Grading Instructions: If all rows have a checkmark in the *No* column, then grade the protocol deviation as **Minor**. If any rows have a checkmark in the *Yes* and/or *Possibly* columns, then grade the protocol deviation as **Moderate/Major**. Circle the appropriate protocol deviation grade on this checklist and add the initial grade to the *CP-CTNet Protocol Deviation Notification* electronic Case Report Form (eCRF) in Medidata Rave.

Initial Protocol Deviation Grade (circle one):

Minor **Moderate/Major**