Date: 1/25/2018
From: Shanda Finnigan, MPH, RN
Subject: CTEP CTCAE v4.0 to CTCAE v5.0 Conversion Amendment Request –
            UPDATE page 3

On March 31, 2018, CTEP IT infrastructure will migrate to CTCAE version 5.0. Effective April 1, 2018, all patient data *submitted to CTEP* must utilize CTCAE v5.0. This applies to **all** current and future CTEP protocols as well as any other protocols utilizing CTEP-AERS, CDUS (Complete or Abbreviated), and/or CTMS Monitoring (ex. DCP NCORP studies).

- CTEP-AERS will automatically reflect CTCAE v5.0 for all SAE reporting.

- CDUS submissions after March 29, 2018 will only be accepted using CTCAE v5.0.

- As with previous CTCAE conversions, CTCAE v5.0 will be required *for submission to CTEP*. Active/Ongoing studies may continue to collect and locally store AE data in CTCAE v4.0, but it must be mapped to CTCAE v5.0 for each quarterly CDUS submission.

CTCAE v5.0 documents, including a mapping document, are available on the CTEP website:
https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm

Revisions/Amendments:

➢ All protocols with a status other than 'Complete', 'Administratively Complete', or 'FDAAA/IRB Completed' must be revised/amended to reference CTCAE v5.0. You may begin submitting revisions/amendments immediately.

➢ Revisions or Amendments must be submitted to the CTEP PIO electronically at pio@ctep.nci.nih.gov.

➢ Amendments with CTCAE as the only change will be treated as editorial and expedited.

➢ Protocol sections which may be affected by the CTCAE update:
  - Patient Selection
  - Treatment
  - Adverse Events
  - Protocol-Specific Exceptions to Expedited Reporting
  - Dose Limiting Toxicities
  - Dose Delays/Modifications
  - Statistical Section
  - Study Oversight/Data Reporting/Regulatory Requirements
  - Other sections not listed above
  - **DO NOT** update the CAEPR unless you have received a new CTCAE v5.0 CAEPR*

➢ The CTEP conversion to CTCAE v5.0 will occur regardless of the approval status of the Revision/Amendment.

Example Protocol Language

(section 10.2 from the CTEP Generic Protocol Template - modify and expand to other sections as needed for your protocol)

Example 1 (protocol with no data collected in v4.0):

10.2   Adverse Event Characteristics

- CTCAE term (AE description) and grade: The descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 will be utilized for AE reporting. All appropriate treatment areas should have access to a copy of the CTCAE version 5.0. A copy of the CTCAE version 5.0 can be downloaded from the CTEP web site http://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm.

Example 2 (currently ongoing protocol transitioning from CTCAE v4.0 to v5.0 with v5.0 start date only):

10.2   Adverse Event Characteristics

- CTCAE term (AE description) and grade: The descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 will be utilized for AE reporting beginning April 1, 2018. All appropriate treatment areas should have access to a copy of the CTCAE version 5.0. A copy of the CTCAE version 5.0 can be downloaded from the CTEP web site http://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm.

Example 3 (currently ongoing protocol transitioning from CTCAE v4.0 to v5.0 with v4.0 end date and v5.0 start date):

10.2   Adverse Event Characteristics

- CTCAE term (AE description) and grade: The descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 will be utilized until March 31, 2018 for AE reporting. CTCAE version 5.0 will be utilized for AE reporting beginning April 1, 2018. All appropriate treatment areas should have access to a copy of the CTCAE version 5.0. A copy of the CTCAE version 5.0 can be downloaded from the CTEP web site http://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm.

*CAEPRS – do not change the CTCAE version within the CAEPR(s) when you amend your study unless you have received a new CTCAE v5.0 CAEPR. CTCAE v5.0 CAEPRs will be sent out as they are updated over the next several months. Most of the CTCAE v5.0 changes do not affect the CAEPR.

→If you use "Find and Replace All" in Word to update v4.0 to v5.0, please make sure you do not change the CAEPR CTCAE version unless you have received a CTCAE v5.0 CAEPR.

Other changes which may affect your protocol: Progressive disease (new term), Pregnancy loss (replaces Fetal death), Death neonatal (updated grading).

Progressive disease Example from CTEP Generic Protocol Template:

10.3.3 <u>Expedited Reporting Guidelines</u>

Use the NCI protocol number and the protocol-specific patient ID assigned during trial registration on all reports.

Note: A death on study requires <u>both</u> routine and expedited reporting, regardless of causality. Attribution to treatment or other cause must be provided.

Death due to progressive disease should be reported as **Grade 5 "Disease progression"** in the system organ class (SOC) "General disorders and administration site conditions." Evidence that the death was a manifestation of underlying disease (*e.g.*, radiological changes suggesting tumor growth or progression: clinical deterioration associated with a disease process) should be submitted.

Pregnancy loss (replacing Fetal death) Example:
Pregnancy loss
- Pregnancy loss is defined in CTCAE as "Death in utero."
- Any Pregnancy loss should be reported expeditiously, as Grade 4 "Pregnancy loss" under the Pregnancy, puerperium and perinatal conditions SOC.
- A Pregnancy loss should NOT be reported as a Grade 5 event under
- the Pregnancy, puerperium and perinatal conditions SOC, as currently CTEPAERS
- recognizes this event as a patient death.

Death neonatal (grade update) Example:
A neonatal death should be reported expeditiously as Grade 4, "Death neonatal" under the General disorders and administration SOC.