COMMON TOXICITY CRITERIA MANUAL

Common Toxicity Criteria, Version 2.0

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Table of Contents

COMMON TOXICITY CRITERIA QUICK REFERENCE

Definition of Adverse Event

- **Toxicity –** Toxicity is NOT clearly defined by regulatory organizations. Toxicity has been described as an adverse event that has an attribution (the relationship to investigational agent) of possible, probable or definite. To minimize confusion, the NCI would recommend that the term toxicity NOT be utilized.

  Note: The Cancer Therapy Evaluation Program, Common Toxicity Criteria, Version 2.0 (CTC, v2.0) uses the term "toxicity" for historical reasons, but recommends that the term "adverse event" with its attribution be used instead whenever possible.

- **Adverse Event** – Any unfavorable symptom, sign, or disease (including an abnormal laboratory finding) temporally associated with the use of a medical treatment or procedure that may or may NOT be considered related to the medical treatment or procedure.

- **Common Toxicity Criteria (CTC)**[1] – The CTC, v2.0 provides descriptive terminology for adverse event reporting. A grading (severity) scale is provided for each adverse event term.

Common Toxicity Criteria (CTC) Categories

- CTC, v2.0 contains 24 categories.
- CTC, v2.0 is organized by pathophysiology and anatomy.
- Alphabetical listings of adverse events are placed within categories.
- The entire CTC, v2.0 should always be available for grading adverse events; however, NCI only requires grading of adverse events that occur.

Changes to the CTC, v2.0

Major changes in the new version of the CTC, v2.0 are outlined in Sections 2.4 and 2.5 of this manual.

[1] All studies reviewed and approved after March 5, 1998 must utilize the CTC version 2.0 standards 1998 for adverse event grading and attribution.

Grades (General Definitions)

- 0 = No adverse event or within normal limits
- 1 = Mild adverse event
- 2 = Moderate adverse event
- 3 = Severe and undesirable adverse event
- 4 = Life-threatening or disabling adverse event
- 5 = Death related to adverse event

The definition of Dose-limiting adverse event is determined by the protocol and not by the CTC.

Grading Adverse Events

- Any treatment-related adverse event experienced by a patient is graded using the specific adverse event terms listed in the CTC, v2.0.
- Grading is not modified based on a patient's condition at baseline. Whenever possible, baseline data, including laboratory data and signs and symptoms noted at study entry, should be collected within the institution as course 0, although at present, there is no electronic reporting capability for baseline data within the Clinical Data Update System (CDUS).
- If a given adverse event is experienced more than once during a cycle, only the grade associated with the most severe adverse event is reported.
- Syndromes are graded only when diagnosed by a physician; notes within the CTC, v2.0 provide guidelines to determine when to grade components of each syndrome.
- Adverse events not included in the CTC, v2.0 should be reported and graded under the "Other" adverse event within the appropriate category and graded 1 to 5 according to the general grade definitions provided above.
- Several adverse events contain notes reminding the investigator of other related adverse events that may occur in association and should be considered for grading.
- Multimodality Therapies – Most adverse events and grading criteria are applicable to any treatment modality. Some are specified for a particular modality. The most relevant adverse event should be used to grade adverse events. When it is not possible to determine whether one or both contributed, use the most relevant description of the adverse event.

Scale for Attribution of Adverse Event

Assign attribution of each adverse event reported in an NCI-sponsored IND study using the following criteria:

ATTRIBUTION OF ADVERSE EVENTS		
Code	**Descriptor**	**Definition**
5	Definite	The adverse event is *clearly related* to the investigational agent(s)
4	Probable	The adverse event is *likely related* to the investigational agent(s)
3	Possible	The adverse event *may be related* to the investigational agent(s)
2	Unlikely	The adverse event is *doubtfully related* to the investigational agent(s)
1	Unrelated	The adverse event is *clearly not related* to the investigational agent(s)

What not to Grade

- Disease progression or signs and symptoms definitely related to disease should not be graded. Objective documentation of progression should always be sought.
- Treatment delivery system malfunctions should not be graded as adverse events.

Options for More Detailed Reporting

When required by the protocol, additional information may be collected using two special modules:

- Adverse Event Module
- Infections Module

Populations and Modalities

When selecting which criteria to use for an adverse event, use the one most consistent with the patient population or treatment modality.

Special criteria for pediatric populations and bone marrow transplant, leukemia, and radiation treatment modalities are shaded in the CTC, v2.0 for easy recognition.

Special Populations

- Pediatrics – Adverse events and adverse event criteria relevant only to children are identified by *italic type* for easy recognition.

Treatment Modalities

- Bone Marrow Transplant Adverse Events – Specialized criteria are included for grading Leukocytes, Platelets, Transfusion: platelets, Transfusion: pRBCs, Weight gain-Veno Occlusive Disease (VOD), Bilirubin-Graft Versus Host

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