Table 24.1 Example of a definition of an adverse event

Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Seizure	Brief partial seizure, no loss of consciousness	Brief generalized seizure	Multiple seizure despite medical intervention	Life-threatening; prolonged repetitive seizures	Death

take the form of the MedDRA dictionary, which may be used for all types of clinical trials, and the CTCAE dictionary, which is used for oncology clinical trials, for adverse events. Medical Dictionary for Regulatory Activities (MedDRA) is a dictionary of adverse events, developed by the International Conference on Harmonization (ICH). The MedDRA dictionary contains over 80,000 terms. In cancer treatment trials, a standard dictionary for use in reporting adverse event data is Common Terminology Criteria for Adverse Events (CTCAE) (160,161). CTCAE was developed by the National Cancer Institute (NCI). The CTCAE (ver. 3) dictionary contains 1,059 terms. The clinician acquires information about the AE, consults the CTCAE, and then transmits the AE using the appropriate term to the data manager (162).

b. CTCAE dictionary

The terms in CTCAE allows for severity grading. For each term, the physician can choose between one of four grades, mild, moderate, severe, or life-threatening (163). The MedDRA system does not allow severity grading. An example of one of CTCAE's definitions is shown in Table 24.1. It is evident that, even though CTCAE is intended for use in oncology clinical trials, the adverse event shown in the table is not an adverse event specifically associated with cancer or with anti-cancer drugs (164).

MedDRA is used for regulatory reporting, while CTCAE is used for publications in oncology journals. Both dictionaries (MedDRA and CTCAE) may be used concurrently for an oncology study that is funded by the National Cancer Institute (NCI), thereby requiring use of CTCAE, and that is used for regulatory approval, where there is the preferred use of MedDRA (165). According to FDA's Guidance for Industry, the FDA does not impose any particular dictionary, but does prefer that the MedDRA dictionary be used, writing, "the FDA prefers that applicants use the

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[161] Trotti A, Colevas AD, Setser A, et al. CTCAE v3.0: development of a comprehensive grading system for the adverse effects of cancer treatment. *Semin Radiat Oncol*. 2003;13:176–181.

[162] Basch E, Jia X, Heller G, et al. Adverse symptom event reporting by patients vs clinicians: relationships with clinical outcomes. *J Natl Cancer Inst*. 2009;101:1624–1632.

[163] Trotti A, Colevas AD, Setser A, Basch E. Patient-reported outcomes and the evolution of adverse event reporting in oncology. *J Clin Oncol*. 2007;25:5121–5127.

[164] Common Terminology Criteria for Adverse Events (CTCAE) Ver. 4.0. May 28, 2009 (v4.03: June 14, 2010).

[165] Trotti A, Colevas AD, Setser A, Basch E. Patient-reported outcomes and the evolution of adverse event reporting in oncology. *J Clin Oncol*. 2007;25:5121–5127.