COMMON TOXICITY CRITERIA (CTC) Version 2.0

NOTICE OF MODIFICATIONS
Modifications made between January 30, 1998 and April 30, 1999

This document provides a description of the modifications made to the *Common Toxicity Criteria Version 2.0* document between January 30, 1998 and April 30, 1999. The majority of the modifications are editorial adjustments that add clarity, consistency or correct typographical errors.

This document describes each modification within a rectangle which points to the location of the modification. Bold text within the rectangle indicates the new value or text. Modifications that are repeated throughout the document are presented with a numeric annotation (see below) to prevent redundancy. Item-specific modifications are described at the point of the modification.

Please note that all grading criteria, *Notes* and *Also consider* details are deleted from this publication to simplify the viewing of this document. The Adverse Event names and the document formatting remain intact to allow for comparisons between this document and CTC document published April 30, 1999.

NUMERIC ANNOTATIONS (Global Modifications)

Used for identifying modifications made for consistency purposes throughout the CTC V2.0 document.

Annotation Number	Modification Description
G1	The word *toxicity* was replaced with the term *adverse event*.
G2	Information now provided within the Adverse Event column was originally presented as a Note relating to the adverse event. Both the adverse event name and the Note were consolidated to condense the information. The phrase *if specified in the protocol* was also added.
G3	The phrase *if specified in the protocol* was added to the adverse event name.
G4	A comma was added to values exceeding four digits.
G5	The unit of measure *cc* was changed to *mL*.
G6	*Note*: changed to *Notes*: where two or more notes appear consecutively.
G7	Minor editorial changes (i.e., punctuation, capitalization and lowercase corrections, replacement of hyphens with colons, etc).

Version 2.0
Publish Date: April 30, 1999

COMMON TOXICITY CRITERIA (CTC)

	Grade				
Adverse Event	**0**	**1**	**2**	**3**	**4**
			ALLERGY/IMMUNOLOGY		
Allergic reaction/ hypersensitivity (including drug fever) Note: Isolated urticaria…					
Allergic rhinitis (including sneezing, nasal stuffiness, postnasal drip)					
Autoimmune reaction Also consider Hypothyroidism...					
Serum sickness					
Urticaria is graded...					
Vasculitis					
Allergy/Immunology - Other (Specify, _____)					
			AUDITORY/HEARING		
Conductive hearing loss is graded...					
Earache is graded...					
External auditory canal Note: Changes associated...					

G1

G1

The organization, document title and date were added to the footer.

Adverse Event	Grade 0	1	2	3	4
Inner ear/hearing					
Middle ear/hearing					
Auditory/Hearing - Other (Specify, _____)					
BLOOD/BONE MARROW					
Bone marrow cellularity					
Normal ranges:					
children (≤ 18 years)					
younger adults (19-59)					
older adults (≥ 60 years)					
Note: Grade Bone...					
CD4 count					
Haptoglobin					
Hemoglobin (Hgb)					
For leukemia studies or bone marrow infiltrative/ myelophthisic processes, if specified in the protocol.					
Hemolysis (e.g., immune hemolytic anemia, drug-related hemolysis, other)					
Also consider Haptoglobin…					

The Grade 1 value for Bone marrow cellularity was changed to **mildly hypocellular or ≤ 25% reduction** ("≤" was added).

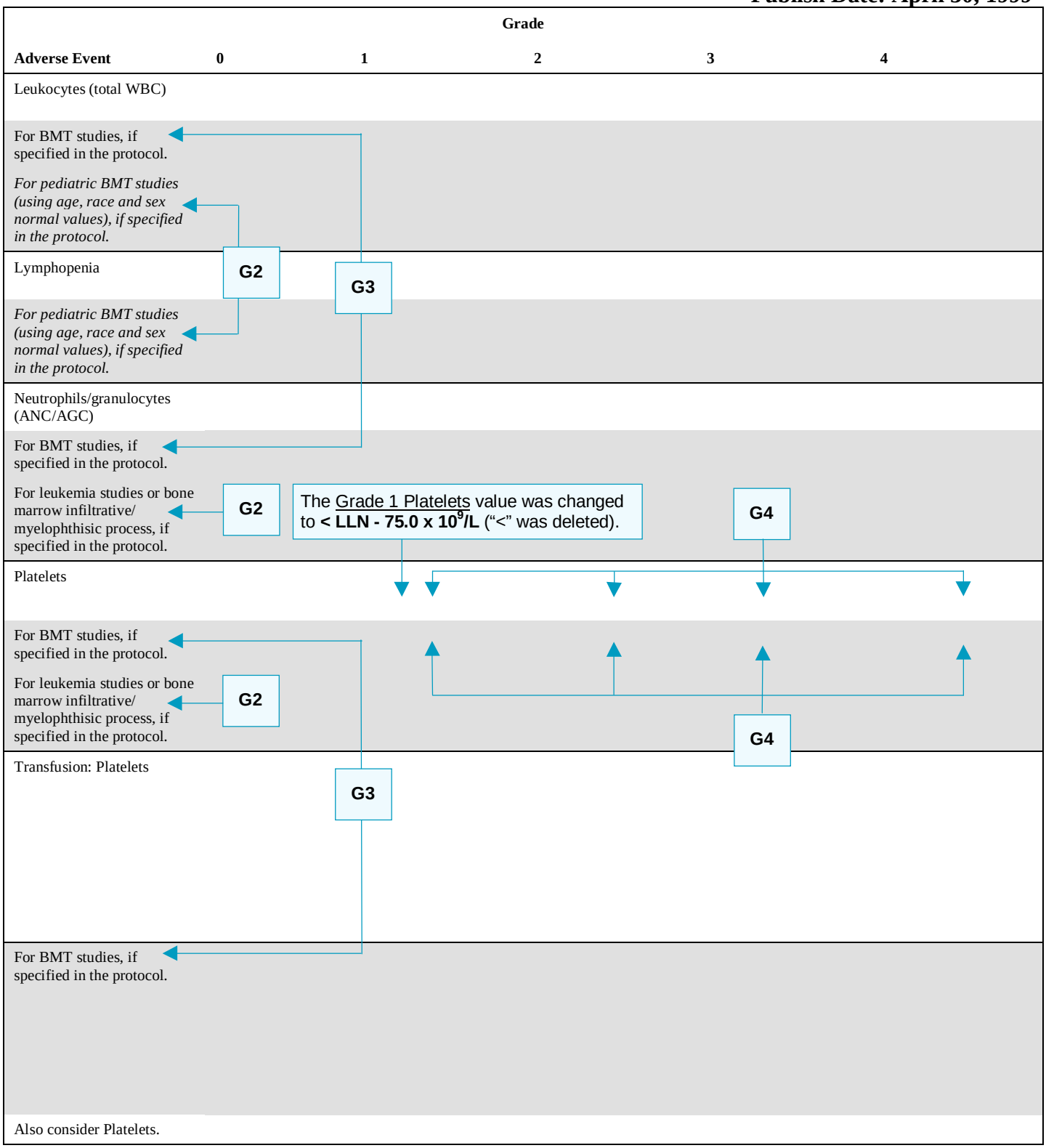
The row listing normal ranges for children was shaded and the text changed to italic to indicate pediatric information.

The value for Grade 3 Hemoglobin was changed to **65 - < 80 g/L** ("<" was added).

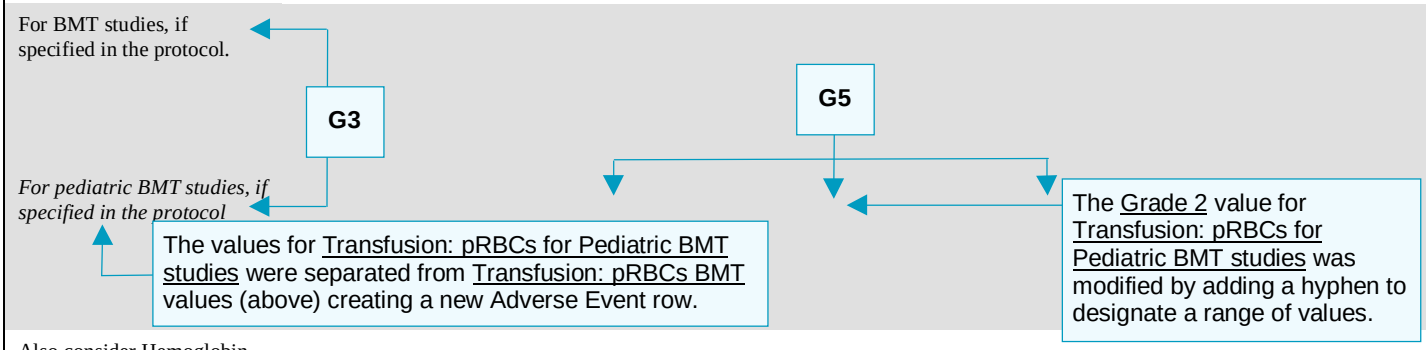
G2

The abbreviation *Hgb* was written in full as **Hemoglobin**.

Version 2.0
Publish Date: April 30, 1999



Adverse Event	Grade 0	1	2	3	4
Transfusion: pRBCs					
For BMT studies, if specified in the protocol.					
For pediatric BMT studies, if specified in the protocol					
Also consider Hemoglobin.					
Blood/Bone Marrow - Other (Specify, _____)					
CARDIOVASCULAR (ARRHYTHMIA)					
Conduction abnormality/ Atrioventricular heart block					
Nodal/junctional arrhythmia/dysrhythmia					
Palpitations Note: Grade palpitations...					
Prolonged QTc interval (QTc > 0.48 seconds)					
Sinus bradycardia					
Sinus tachycardia					
Supraventricular arrhythmias (SVT/atrial fibrillation/ flutter)					
Syncope (fainting) is...					
Vasovagal episode					



Adverse Event	Grade 0	1	2	3	4
Ventricular arrhythmia (PVCs/bigeminy/trigeminy/ ventricular tachycardia)					
Cardiovascular/ Arrhythmia - Other (Specify, _____)					
CARDIOVASCULAR (GENERAL)					
Acute vascular leak syndrome					
Cardiac-ischemia/infarction					
Cardiac left ventricular function					
CNS cerebrovascular ischemia is...					
Cardiac troponin I (cTnI)					
Cardiac troponin T (cTnT)					
Edema					
Hypertension **Note: For pediatric patient...*					

	Grade				
Adverse Event	**0**	**1**	**2**	**3**	**4**
Hypotension Also consider Syncope (fainting). Notes: Angina or MI is graded... *For pediatric patients…*					
Myocarditis					
Operative injury of vein/artery					
Pericardial effusion/ pericarditis					
Peripheral arterial ischemia					
Phlebitis (superficial) Notes: Injection... Thrombosis/embolism...					
Syncope (fainting) is...					
Thrombosis/embolism					
Vein/artery operative injury is...					
Visceral arterial ischemia (non-myocardial)					
Cardiovascular/ General - Other (Specify, _____)					

G6

The Grade 3 criterion for Pericardial effusion/pericarditis was revised to ***with physiologic consequences*** ("resulting from symptoms" deleted).

Adverse Event	Grade 0	1	2	3	4
COAGULATION					
Note: See the HEMORRHAGE...					
DIC (disseminated intravascular coagulation) Also consider Platelets. Note: Must have…					
Fibrinogen					
For leukemia studies or bone marrow infiltrative/ myelophthisic process, if specified in the protocol.					
Partial thromboplastin time (PTT)					
Phlebitis is graded...					
Prothrombin time (PT)					
Thrombosis/embolism is graded...					
Thrombotic microangiopathy (e.g., thrombotic thrombocytopenic purpura/TTP or hemolytic uremic syndrome/HUS)					
For BMT studies, if specified in the protocol.					
Also consider Hemoglobin... Note: Must have...					
Coagulation - Other (Specify, _____)					
CONSTITUTIONAL SYMPTOMS					
Fatigue (lethargy, malaise, asthenia) Note: See Appendix III...					

The word *grade* was replaced with the word **consider**.

The Grade 4 value for Fibrinogen for leukemia studies or bone marrow infiltrative/ myelophthisic process was changed to **<50mg** ("%" was deleted).

G2

The spelling for the word **Phlebitis** was corrected.

G3

Adverse Event	Grade 0	1	2	3	4
Fever (in the absence of neutropenia, where neutropenia is defined as AGC < 1.0 x 10^9/L) Also consider Allergic... Note: The temperature...					
Hot flashes/flushes...					
Rigors, chills					
Sweating (diaphoresis)					
Weight gain Also consider Ascites…					
Weight gain associated with Veno-Occlusive Disease (VOD) for BMT studies, if specified in the protocol.					
Also consider Ascites…					
Weight loss Also consider Vomiting...					
Constitutional Symptoms - Other (Specify, _____)					
DERMATOLOGY/SKIN					
Alopecia					
Bruising (in absence of grade 3 or 4 thrombocytopenia) Note: Bruising resulting...					
Dry skin					
Erythema multiforme (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis)					
Flushing					
Hand-foot skin reaction					
Injection site reaction					

The Also consider for Weight gain was changed to include the term Pleural effusion **(non-malignant)**.

G2

G7

The spelling for the word **ascites** was corrected.

The Also consider **Ascites, Edema, Pleural effusion (non-malignant)** was added to Weight gain associated with Veno-Occlusive Disease for BMT studies.

The adverse event Dermatitis, focal (associated with high-dose chemotherapy and bone marrow transplant) originally listed between Bruising and Dry skin was renamed **Rash/dermatitis** and moved to page 9.

Adverse Event	Grade 0	1	2	3	4
Nail changes					
Petechiae is graded…					
Photosensitivity					
Pigmentation changes (e.g., vitiligo)					
Pruritus					
Purpura is graded...					
Radiation dermatitis Note: Pain associated...					
Radiation recall reaction (reaction following chemotherapy in the absence of additional radiation therapy that occurs in a previous radiation port)					
Rash/desquamation Also consider Allergic reaction/hypersensitivity. Note: Stevens-Johnson syndrome...					
Rash/dermatitis associated with high-dose chemotherapy or BMT studies. Rash/desquamation associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol. Also consider Allergic reaction/hypersensitivity. Note: Stevens-Johnson syndrome...					

G7

The Note for Rash/desquamation was changed to **Stevens-Johnson syndrome is graded separately as Erythema multiforme in the DERMATOLOGY/SKIN category**.

Dermatitis, focal was renamed **Rash/dermatitis associated with high-dose chemotherapy or BMT studies** and moved under Rash/desquamation (see page 8 for details).

G2

The event name for Rash/desquamation for BMT was revised to **Rash/ desquamation associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol.**

The spelling for the word **pruritus** was corrected.

Adverse Event	Grade 0	1	2	3	4
Urticaria (hives, welts, wheals)					
Wound-infectious					
Wound-non-infectious					
Dermatology/Skin - Other (Specify, _____)					
ENDOCRINE					
Cushingoid appearance (e.g., moon face, buffalo hump, centripetal obesity, cutaneous striae)					
Also consider Hyperglycemia...					
Feminization of male					
Gynecomastia					
Hot flashes/flushes					
Hypothyroidism					
Masculinization of female					
SIADH (syndrome of inappropriate antidiuretic hormone)					
Endocrine - Other (Specify, _____)					
GASTROINTESTINAL					
Amylase is graded in the METABOLIC/LABORATORY category.					
Anorexia					
Ascites (non-malignant)					
Colitis					
Also consider Hemorrhage...					
Constipation					

The spelling for the word ***fasciitis*** was corrected.

The exempli gratia (e.g.) for Cushingoid appearance was changed to **e.g., moon face, buffalo hump, centripetal obesity, cutaneous striae** ("with or without" was deleted).

	Grade				
Adverse Event	**0**	**1**	**2**	**3**	**4**
Dehydration Also consider Diarrhea...					
Diarrhea Patients without colostomy: Patients with a colostomy:					
Diarrhea associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol. *For Pediatric BMT studies, if specified in the protocol.*					
Also consider Hemorrhage...					
Duodenal ulcer (requires radiographic or endoscopic documentation)					
Dyspepsia/heartburn					
Dysphagia, esophagitis, odynophagia (painful swallowing) Note: If the adverse event is...					
Dysphagia-esophageal related to radiation Also consider Pain Note: Fistula is...					
Dysphagia-pharyngeal related to radiation Also consider Pain due... Note: Fistula is graded...					
Fistula-esophageal					
Fistula-intestinal					

The Also Consider for Dehydration was changed to **Diarrhea, Vomiting, Stomatitis/pharyngitis (oral/ pharyngeal mucositis), Hypotension** ("Hypotension" moved to the end of the sentence).

The event Diarrhea for BMT studies was changed to **Diarrhea associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol**.

G3

The Also Consider for Diarrhea was changed by removing the row shading to indicate that it relates to all four (4) Diarrhea adverse events.

G1

G7

	Grade				
Adverse Event	**0**	**1**	**2**	**3**	**4**
Fistula-pharyngeal					
Fistula-rectal/anal					
Flatulence					
Gastric ulcer (requires radiographic or endoscopic documentation) Also consider Hemorrhage/...					
Gastritis Also consider Hemorrhage...					
Hematemesis is graded...					
Hematochezia is graded...					
Ileus (or neuroconstipation)					
Mouth dryness					
Mucositis Notes: Mucositis not due to radiation... Radiation-related mucositis...					
Mucositis due to radiation Also consider Pain due to radiation. Notes: Grade radiation mucositis… Dysphagia related to...					
Nausea					
Pancreatitis Also consider Hypotension. Note: Amylase...					
Pharyngitis is graded...					

G6

The spelling for the word **Vaginitis** was corrected.

G6

The Note for Pancreatitis was revised to **Amylase is graded in the METABOLIC/LABORATORY category** ("Asymptomatic Amylase and" was deleted).

Adverse Event	Grade 0	1	2	3	4
Proctitis			G7		
Also consider Hemorrhage... Notes: Fistula is graded... Proctitis occurring...			G6		
Salivary gland changes			G7		
Sense of smell					
Stomatitis/pharyngitis (oral/pharyngeal mucositis)					
For BMT studies, if specified in the protocol.			G3		
Note: Radiation-related mucositis...					
Taste disturbance (dysgeusia)					
Typhlitis (inflammation of the cecum)					
Also consider Hemorrhage/...					
Vomiting				G7	
Also consider Dehydration.					
Weight gain is graded in…					
Weight loss is graded in...					
Gastrointestinal – Other (Specify, _____)					

The Also consider for Proctitis was changed to **Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia, Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia, Pain due to radiation** (the word "and" was deleted).

The spelling for the word ***prophylactic*** was corrected.

The Grade 3 criteria for Typhlitis was revised to **abdominal pain, diarrhea, fever, and radiographic or biopsy documentation.**

The term Febrile/neutropenia in the Also consider for Typhlitis was changed to Febrile neutropenia ("/" was deleted).

Version 2.0
Publish Date: April 30, 1999

Adverse Event	Grade 0	1	2	3	4
HEMORRHAGE					
Notes: Transfusion in this...					
For any bleeding with...					
If the site or type of Hemorrhage...					
If the platelet...					
Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia					
Also consider Platelets...					
Note: This adverse event must...					
Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia					
Also consider Platelets...					
Note: Bleeding in...					
CNS hemorrhage/bleeding					
Epistaxis					
Hematemesis					
Hematuria (in the absence of vaginal bleeding)					
Hemoptysis					
Hemorrhage/bleeding associated with surgery					
Note: Expected blood loss...					
Melena/GI bleeding					

G6

G7

The Note beginning with "For any bleeding with…" was revised to …**in addition to grading severity by grading the site or type of bleeding.**

G7

The Also consider for Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia was revised to ***Platelets, Hemoglobin, Transfusion-platelets, Transfusion-pRBCs site or type of bleeding. If the site is not listed, grade as Hemorrhage-Other (Specify site, _____).***

G1

The Note for Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia was revised by deleting the sentence "Also grade the site or type of hemorrhage/ bleeding. If the site is not listed, grade as Other in the HEMORRHAGE category".

G7

The Also consider for Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia was revised by adding **Hemorrhage-Other (Specify site, _____)**.

G1

Adverse Event	Grade 0	1	2	3	4
Petechiae/purpura (hemorrhage/bleeding into skin or mucosa)					
Rectal bleeding/ hematochezia					
Vaginal bleeding					
Hemorrhage - Other (Specify site, _____)					
HEPATIC					
Alkaline phosphatase					
Bilirubin					
Bilirubin associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol.					
GGT (γ - Glutamyl transpeptidase)					
Hepatic enlargement					
Note: Grade Hepatic...					
Hypoalbuminemia					
Liver dysfunction/ failure (clinical)					
Portal vein flow					
SGOT (AST) (serum glutamic oxaloacetic transaminase)					
SGPT (ALT) (serum glutamic pyruvic transaminase)					
Hepatic - Other (Specify, _____)					
INFECTION/FEBRILE NEUTROPENIA					
Catheter-related infection					

G2

The rows for Hepatic enlargement and its Note were shaded to indicate the relationship between VOD and BMT.

G1

The Note for Hepatic enlargement was revised to **Grade Hepatic enlargement only for treatment related adverse event including Veno-Occlusive Disease.**

The Note for Liver dysfunction/failure (clinical) was deleted.

Adverse Event	Grade 0	1	2	3	4
Febrile neutropenia (fever of unknown origin without clinically or microbiologically documented infection) (ANC < 1.0 x 10^9/L, fever ≥38.5°C) Also consider Neutrophils. Note: Hypothermia instead…					
Infection (documented clinically or microbiologically) with grade 3 or 4 neutropenia (ANC < 1.0 x 10^9/L) Also consider Neutrophils. Notes: Hypothermia instead... In the absence of...					
Infection with unknown ANC Note: This adverse event criterion...					
Infection without neutropenia					
Also consider Neutrophils.					
Wound-infectious is...					
Infection/Febrile Neutropenia - Other (Specify, _____)					
LYMPHATICS					
Lymphatics					
Lymphatics - Other (Specify, _____)					
METABOLIC/LABORATORY					
Acidosis (metabolic or respiratory)					
Alkalosis (metabolic or respiratory)					
Amylase					
Bicarbonate					

The Also consider for Febrile neutropenia was added.

The Also consider for Infection was added.

G6

The Note for Infection (documented clinically or microbiologically) beginning with "In the absence of…" was revised to ***In the absence of documented infection grade 3 or 4 neutropenia with fever is graded as Febrile neutropenia.***

G1

The Also consider for Infection without neutropenia was added.

The Infection/Febrile Neutropenia - Other (Specify, _____) event was moved to appear as the last listing in the INFECTION/FEBRILE NEUTROPENIA Category.

Adverse Event	Grade 0	1	2	3	4
CPK (creatine phosphokinase)					
Hypercalcemia					
Hypercholesterolemia					
Hyperglycemia					
Hyperkalemia					
Hypermagnesemia					
Hypernatremia					
Hypertriglyceridemia					
Hyperuricemia					
Also consider Tumor lysis...					
Hypocalcemia					
Hypoglycemia					
Hypokalemia					
Hypomagnesemia					
Hyponatremia					
Hypophosphatemia					
Hypothyroidism is graded in...					
Lipase					
Metabolic/Laboratory - Other (Specify, _____)					
MUSCULOSKELETAL					
Arthralgia is...					
Arthritis					

The Grade 4 criteria for Hyperglycemia was revised to >500 mg/dL >27.8 mmol/L or **acidosis** ("*ketoacidosis" was deleted*).

The Also consider for Hyperuricemia was revised by replacing the word *Potassium* with ***Hyperkalemia.***

Adverse Event	Grade 0	1	2	3	4
Muscle weakness (not due to neuropathy)					
Myalgia [tenderness or pain...					
Myositis (inflammation/damage of muscle) Also consider CPK. Note: Myositis implies...					
Osteonecrosis (avascular necrosis)					
Musculoskeletal – Other (Specify, _____)					
NEUROLOGY					
Aphasia, receptive and/or...					
Arachnoiditis/meningismus/ radiculitis Also consider Headache...					
Ataxia (incoordination)					
CNS cerebrovascular ischemia					
CNS hemorrhage/bleeding is graded...					
Cognitive disturbance/ learning problems					

The grading instructions for Myalgia was revised to **Myalgia [tenderness or pain in muscles] is graded in the PAIN category.**

	Grade				
Adverse Event	**0**	**1**	**2**	**3**	**4**
Confusion					
Cranial neuropathy is graded in...					
Delusions					
Depressed level of consciousness Note: Syncope (fainting)...					
Dizziness/lightheadedness					
Dysphasia, receptive and/or...					
Extrapyramidal/ involuntary movement/ restlessness					
Hallucinations					
Headache is graded in the PAIN...					
Insomnia Note: This adverse event is… ← **G1**					
Irritability (children <3 years of age)					
Leukoencephalopathy associated radiological findings ← The italics and row shading were removed from the Leukoencephalopathy associated radiological findings event.					
Memory loss					

	Grade				
Adverse Event	**0**	**1**	**2**	**3**	**4**
Mood alteration-anxiety, agitation	G7				
Mood alteration-depression					
Mood alteration-euphoria					
Neuropathic pain is graded...					
Neuropathy-cranial					
Neuropathy-motor					
Neuropathy-sensory					
Nystagmus Also consider Vision-double...					
Personality/behavioral					
Pyramidal tract dysfunction (e.g., ↑ tone, hyperreflexia, positive Babinski, ↓ fine motor coordination)					
Seizure(s)					
Speech impairment (e.g., dysphasia or aphasia)					
Syncope (fainting) Also consider CARDIOVASCULAR...					

Adverse Event	Grade 0	1	2	3	4
Tremor					
Vertigo					
Neurology - Other (Specify, _____)					
OCULAR/VISUAL					
Cataract					
Conjunctivitis					
Dry eye					
Glaucoma					
Keratitis (corneal inflammation/ corneal ulceration)					
Tearing (watery eyes)					
Vision-blurred vision					
Vision-double vision (diplopia)					
Vision-flashing lights/floaters					

Adverse Event	Grade 0	1	2	3	4
Vision-night blindness (nyctalopia)					
Vision-photophobia					
Ocular/Visual - Other (Specify, _____)					
PAIN					
Abdominal pain or cramping					
Arthralgia (joint pain)					
Arthritis (joint pain...					
Bone pain					
Chest pain (non-cardiac and non-pleuritic)					
Dysmenorrhea					
Dyspareunia					
Dysuria is graded in the...					
Earache (otalgia)					
Headache					

Adverse Event	Grade 0	1	2	3	4
Hepatic pain					
Myalgia (muscle pain)					
Neuropathic pain (e.g., jaw pain, neurologic pain, phantom limb pain, post-infectious neuralgia, or painful neuropathies)					
Pain due to radiation					
Pelvic pain					
Pleuritic pain					
Rectal or perirectal pain (proctalgia)					
Tumor pain (onset or exacerbation of tumor pain due to treatment)					
Tumor Flare is...					
Pain - Other (Specify, _____)					
PULMONARY					
Adult Respiratory Distress Syndrome (ARDS)					
Apnea					

The spelling for the word ***flare*** was corrected.

	Grade				
Adverse Event	**0**	**1**	**2**	**3**	**4**
Carbon monoxide diffusion capacity (DL_{CO})					
Cough					
Dyspnea (shortness of breath)					
FEV_1					
Hiccoughs (hiccups, singultus)					
Hypoxia					
Pleural effusion (non-malignant)					
Pleuritic pain is graded in the...					
Pneumonitis/pulmonary infiltrates					
Pneumothorax					
Pulmonary embolism is…					
Pulmonary fibrosis					
Note: Radiation-related pulmonary...					
Voice changes/stridor/larynx (e.g., hoarseness, loss of voice, laryngitis)					
Notes: Cough from...  Radiation-related hemoptysis...					
Pulmonary – Other (Specify, _____)					

Adverse Event	Grade 0	1	2	3	4
RENAL/GENITOURINARY					
Bladder spasms					
Creatinine *Note: Adjust to age-appropriate…*					
Dysuria (painful urination)					
Fistula or GU fistula (e.g., vaginal, vesicovaginal)					
Hemoglobinuria					
Hematuria (in the absence of vaginal...					
Incontinence					
Operative injury to bladder and/or ureter					
Proteinuria Note: If there is an inconsistency between absolute...					
Renal failure					
Ureteral obstruction					
Urinary electrolyte wasting (e.g., Fanconi's syndrome, renal tubular acidosis) Also consider Acidosis,...					
Urinary frequency/urgency					
Urinary retention					

The spelling for the word **antispasmodic** was corrected.

The Note for Proteinuria was revised by replacing *Uristix* with **dip stick.**

Adverse Event	Grade 0	1	2	3	4
Urine color change (not related to other dietary or physiologic cause e.g., bilirubin, concentrated urine, hematuria)					
Vaginal bleeding is graded...					
Vaginitis (not due to infection)					
Renal/Genitourinary - Other (Specify, _____)					
SECONDARY MALIGNANCY					
Secondary Malignancy - Other (Specify type, _____) excludes metastasis from initial primary					
SEXUAL/REPRODUCTIVE FUNCTION					
Dyspareunia is...					
Dysmenorrhea is…					
Erectile impotence					
Female sterility					
Feminization of...					
Irregular menses (change from baseline)					
Libido					
Male infertility					
Masculinization of female is...					
Vaginal dryness					
Sexual/Reproductive Function - Other (Specify, _____)					
SYNDROMES (not included in previous categories)					
Acute vascular leak syndrome...					
ARDS (Adult Respiratory Distress...					

The Secondary Malignancy - Other (Specify type, ____) was revised to include **excludes metastasis from initial primary.**

The spelling for the word **feminization** was corrected.

G7

	Grade				
Adverse Event	**0**	**1**	**2**	**3**	**4**
Autoimmune reactions are graded...					
DIC (disseminated intravascular...					
Fanconi's syndrome is graded as...					
Renal tubular acidosis is graded...					
Stevens-Johnson syndrome...					
SIADH (syndrome of inappropriate…					
Thrombotic microangiopathy...					
Tumor flare Also consider Hypercalcemia. Note: Tumor flare...					
Tumor lysis syndrome Also consider...					
Urinary electrolyte...					
Syndromes - Other (Specify, _____)		mild	moderate	severe	life-threatening or disabling

The spelling for the word **thrombotic** was corrected.

The spelling for the word **syndrome** was corrected.

G7

Appendix I

Adverse Event Module

To be implemented at the request of the study sponsor or principal investigator in the protocol or by protocol amendment when more detailed information is considered pertinent.

Adverse Event:	Date of Treatment:	Course Number:
Date of onset:		Grade at onset:
Date of first change in grade:		Grade:
Date of next change in grade:		Grade:
Date of next change in grade:		Grade:
Date of next change in grade:		Grade:
Date of next change in grade:		Grade:
Date of next change in grade:		Grade:
Did adverse event resolve? If so, date of resolution of adverse event:	Yes_____	No_____
Date of last observation (if prior to recovery):		
Reason(s) observations stopped (if prior to recovery):		
Was patient retreated?	Yes_____	No_____
If yes, was treatment delayed for recovery?	Yes_____	No_____
Date of next treatment?		
Dose reduced for next treatment?	Yes_____	No_____

Additional Comments:

_____

_____

If module is being activated for new adverse event not currently in CTC, please provide definitions for adverse event grading:

Grade 0 = _____

Grade 1 = _____

Grade 2 = _____

Grade 3 = _____

Grade 4 = _____

Appendix II

Infection Module

To be implemented at the request of the study sponsor or principal investigator in the protocol or by protocol amendment when more detailed information is considered pertinent.

1. Use the Common Toxicity Criteria definitions to grade the severity of the infection.
2. Specify type of infection from the following (CHOOSE ONE):

   BACTERIAL FUNGAL PROTOZOAL VIRAL UNKNOWN
3. Specify site of infection from the following (CHOOSE ALL THAT APPLY):

   BLOOD CULTURE POSITIVE
   BONE INFECTION
   CATHETER (intravenous)
   CATHETER (intravenous), tunnel infection
   CENTRAL NERVOUS SYSTEM INFECTION
   EAR INFECTION
   EYE INFECTION
   GASTROINTESTINAL INFECTION
   ORAL INFECTION
   PNEUMONIA
   SKIN INFECTION
   UPPER RESPIRATORY INFECTION
   URINARY TRACT INFECTION
   VAGINAL INFECTION
   INFECTION, not otherwise specified (Specify site, _____)
4. Specify organism, if known: _____.
5. Prophylactic antibiotic, antifungal, or antiviral therapy administration

   Yes_____ No_____

   If prophylaxis was given prior to infection, please specify below:

   Antibiotic prophylaxis _____

   Antifungal prophylaxis _____

   Antiviral prophylaxis _____

   Other prophylaxis _____

Appendix III

Performance Status Scales/Scores

The Performance Status Scale/Scores was revised.

PERFORMANCE STATUS CRITERIA

Karnofsky and Lansky performance scores are intended to be multiples of 10.

ECOG (Zubrod)		Karnofsky		Lansky*	
Score	Description	Score	Description	Score	Description
0	Fully active, able to carry on all pre-disease performance without restriction.	100	Normal, no complaints, no evidence of disease.	100	Fully active, normal.
		90	Able to carry on normal activity; minor signs or symptoms of disease.	90	Minor restrictions in physically strenuous activity.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	80	Normal activity with effort; some signs or symptoms of disease.	80	Active, but tires more quickly
		70	Cares for self, unable to carry on normal activity or do active work.	70	Both greater restriction of and less time spent in play activity.
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	60	Requires occasional assistance, but is able to care for most of his/her needs.	60	Up and around, but minimal active play; keeps busy with quieter activities.
		50	Requires considerable assistance and frequent medical care.	50	Gets dressed, but lies around much of the day; no active play; able to participate in all quiet play and activities.
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	40	Disabled, requires special care and assistance.	40	Mostly in bed; participates in quiet activities.
		30	Severely disabled, hospitalization indicated. Death not imminent.	30	In bed; needs assistance even for quiet play.
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	20	Very sick, hospitalization indicated. Death not imminent.	20	Often sleeping; play entirely limited to very passive activities.
		10	Moribund, fatal processes progressing rapidly.	10	No play; does not get out of bed.

*The conversion of the Lansky to ECOG scales is intended for NCI reporting purposes only.

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Appendix IV

RTOG/EORTC Late Radiation Morbidity Scoring Scheme

Use for adverse event occurring greater than 90 days after radiation therapy.

The spelling for the word **occurring** corrected.

Adverse Event	0	G1	1	2	3	4
Bladder- Late RT Morbidity Scoring						G5
Bone- Late RT Morbidity Scoring						
Brain- Late RT Morbidity Scoring						
Esophagus- Late RT Morbidity Scoring						
Eye- Late RT Morbidity Scoring						
Heart- Late RT Morbidity Scoring						
Joint- Late RT Morbidity Scoring						
Kidney- Late RT Morbidity Scoring						
Larynx- Late RT Morbidity Scoring						

The Eye Late RT Morbidity Scoring was moved to retain the alphabetical order of this appendix.

Appendix IV (continued)

RTOG/EORTC Late Radiation Morbidity Scoring Scheme

Use for adverse event occurring greater than 90 days after radiation therapy.

G1

The spelling for the word **occurring** was corrected.

Adverse Event	0	1	2	3	4
Liver- Late RT Morbidity Scoring					
Lung- Late RT Morbidity Scoring					
Mucous membrane- Late RT Morbidity Scoring					
Salivary glands- Late RT Morbidity Scoring					
Skin- Late RT Morbidity Scoring					
Small/Large intestine- Late RT Morbidity Scoring					
Spinal cord- Late RT Morbidity Scoring					
Subcutaneous tissue- Late RT Morbidity Scoring					
Radiation - Other (Specify, _____)					

Appendix V

BMT-Specific Adverse Events

The BMT-Specific Adverse Events was added to summarize all BMT events included in the CTC v2.0.

Summary of BMT-Specific Adverse Events that may be used if specified by the protocol. These differ from the standard CTC and may be more relevant to the transplant setting. They are listed here for the convenience of investigators writing transplant protocols. They are also included in the CTC document.

	Grade				
Adverse Event	**0**	**1**	**2**	**3**	**4**
Bilirubin associated with graft versus host disease for BMT studies.					
Diarrhea associated with graft versus host disease (GVHD) for BMT studies.					
Diarrhea for Pediatric BMT studies.					
Hepatic enlargement					
Leukocytes (total WBC) for BMT studies.					
Leukocytes (total WBC) for pediatric BMT studies (using age, race and sex normal values).					
Lymphopenia for pediatric BMT studies (using age, race and sex normal values).					
Neutrophils/granulocytes (ANC/AGC) for BMT studies.					
Platelets for BMT studies.					
Rash/dermatitis associated with high-dose chemotherapy or BMT studies.					
Rash/desquamation associated with graft versus host disease (GVHD) for BMT studies.					

Appendix V (Continued)

BMT-Specific Adverse Events

Summary of BMT-Specific Adverse Events that may be used if specified by the protocol. These differ from the standard CTC and may be more relevant to the transplant setting. They are listed here for the convenience of investigators writing transplant protocols. They are also included in the CTC document.

	Grade				
Adverse Event	**0**	**1**	**2**	**3**	**4**
Stomatitis/pharyngitis (oral/pharyngeal mucositis) for BMT studies.					
Transfusion: Platelets for BMT studies.					
Transfusion: pRBCs for BMT studies.					
Transfusion: pRBCs for Pediatric BMT studies.					
Thrombotic microangiopathy (e.g., thrombotic thrombocytopenic purpura/TTP or hemolytic uremic syndrome/HUS) for BMT studies.					
Weight gain associated with Veno-Occlusive Disease (VOD) for BMT studies.					

Appendix VI

BMT Complex/Multicomponent Events

Adverse Event	Grade 0	G1	1	2	3	4
Note: The grading of...						
Failure to engraft Also consider Hemoglobin...						
Graft versus host disease Also consider Fatigue...						
Stem cell infusion complications Also consider...						
Veno-Occlusive Disease (VOD) Also consider Weight...						

The list of adverse events included for each Also consider was expanded to include leukemia, pediatric and BMT events, when appropriate.