Manual for the Completion of CDISC Aligned NCI Standard Case Report Form (CRF) Modules

Introduction

In 2006, members of the National Cancer Institute's Center for Biomedical Informatics and Information Technology (NCI CBIIT) in conjunction with the cancer Data Standards Registry and Repository (caDSR) user community initiated a Case Report Form (CRF) harmonization activity. CRFs submitted from the community were reviewed and inventoried. The Harmonization group then reviewed all questions on the CRF and partitioned them into four categories:

- Mandatory A data collection variable that must be on the CRF (e.g., a regulatory requirement (if applicable)).
- Conditional A data collection variable that must be collected on the CRF for specific cases that may be dictated by local or sponsor defined business rules.
- Optional A data collection variable that is available for use if needed. There is no
 regulatory or business requirement for inclusion of this element on the CRF; if the design
 and scientific questions posed in the study dictate the need to collect this type of data;
 this is the element to include on the CRF.
- Non-harmonized A data collection variable that is, by consensus, to primarily belong to a different CRF module or is not belonging to any defined module.

A template form with modules that contain questions or variables representing data to be collected and a companion electronic CRF instruction manual was developed. These CRF modules were vetted and adopted by the caDSR stakeholder community as metadata standards.

Since the original CRFs and manuals were adopted, the Food & Drug Administration (FDA) published guidelines for submission of clinical trial study data using the Clinical Data Interchange Standards Consortium (CDISC) Study Data Tabulation Model (SDTM) for Investigational New Drug (IND) trials starting after December 2017. In response, NCI CBIIT has aligned the NCI Standard CRF modules with the CDISC data collection standard, Clinical Data Acquisition Standards Harmonization (CDASH) where data is expected to be submitted to FDA in SDTM format.

The instruction manual is a set of directions to guide data collection in each module template. Specific implementation instructions are not present; various groups may wish to implement the contents of a module in a variety of software applications.

The instructions include the field name, description or definition of each field, and any special formatting notes that apply to entries – such as the inclusion of full dates, use of values from a choice list only, etc. Finally, each question (or data item) is noted as Mandatory (m), Conditional (c), or Optional (o).

Adverse Event/Serious Adverse Event CTCAE v4.0 CDISC Aligned NCI Standard Template Module Definitions

Mapping to the CDASH:

This NCI Standard Template Form maps to the following domains in the CDASHIG v2.0 metadata table:

- AE Adverse Events (v2.0)
- CO Comments (v2.0)

Mapping to the SDTM:

This NCI Standard Template Form maps to the following domains in the SDTMIG v3.3 metadata table:

- AE Adverse Events (v3.3)
- CO Comments (v3.3)

Adverse Event/Serious Adverse Event CTCAE v4.0 CDISC Aligned NCI Standard Template Module Template Instructions

Field Descriptions and Instructions

Field Name (Partition Status) CDE ID # Short Name	Definition CDISC Mapping and Instruction	Format
Adverse Event MedDRA Low Level Term Version 4 Name (m) 6981742 AELLT4NM	The name of the reported MedDRA version 4 low level term. CDASH: AELLT (6355960) Subset of Adverse Event MedDRA Low Level Term; SDTM: AELLT (No CDE)	CHARACTER
Adverse Event Reported Term (m) 6338308 AETERM	The reported or pre-specified name of the adverse event. CDASH: AETERM (6338308); SDTM: AETERM (No CDE)	CHARACTER
Adverse Event Toxicity Grade (m) 6981800 AEAESVGD	The numeric representation of the severity of the reported adverse event using a standard toxicity scale (such as the NCI CTCAE). CDASH: AETOXGR (6338618); SDTM: AETOXGR (No CDE)	CHARACTER. Use choice list.

Field Name (Partition Status) CDE ID # Short Name	Definition CDISC Mapping and Instruction	Format
Adverse Event Start Date (c) 6341142 AESTDAT	The start date of the adverse event represented in an unambiguous date format (e.g., DD-MON-YYYY).	DATE
	CDASH: AELLT (6355960) Subset of Adverse Event MedDRA Low Level Term; SDTM: AELLT (No CDE) CDASH: AESTDAT (6341142); SDTM: AESTDTC (No CDE); Conditionality Rule: Condition is that this is based on the needs of the Sponsor. CTEP does not currently collect Adverse Event onset dates for routine AEs reported via reporting systems.	
Initial or Prolonged Hospitalization (c) 6343376	An indication the serious adverse event resulted in an initial or prolonged hospitalization.	CHARACTER. Use choice list.
AESHOSP	CDASH: AESHOSP (6343376); SDTM: AESHOSP (No CDE); Conditionality Rule: Conditional based on the reporting of this variable through other means, such as caAERS, AdEERS. If those systems are not in use, this variable needs to be collected.	
Therapeutic Procedure Cycle Number (c) 6981801 ECTXCYNU	The numeric representation of a round of therapeutic treatment that may contain more than one cycle.	NUMBER
	CDASH: No Match; SDTM: No Match; Conditionality Rule: Studies use cycles.	
Therapeutic Procedure Or Disease or Disorder Attribution Type (o)	The treatment modality or disease associated as a cause of the event.	CHARACTER. Use choice list.
6981806 AEATRBTP	CDASH: No Match; SDTM: No Match	

Field Name (Partition Status) CDE ID # Short Name	Definition CDISC Mapping and Instruction	Format
Therapeutic Procedure Or Disease or Disorder Attribution Text (o) 6981833 AEATBTPX	The treatment modality or disease associated as a cause of the event not previously listed. CDASH: No Match; SDTM: No Match	CHARACTER
Adverse Event End Date (o) 6340298 AEENDAT	The date when the adverse event resolved/ended represented in an unambiguous date format (e.g., DD-MON-YYYY). CDASH: AEENDAT (6340298); SDTM: AEENDTC (No CDE)	DATE
Adverse Event Adverse Event MedDRA System Organ Class Name (o) 6981807 AEMSOCNM	The name of the MedDRA Primary System Organ Class associated with the event. CDASH: AESOC (6380294); SDTM: AEBODSYS(6658533)	CHARACTER. Use choice list.
Adverse Event MedDRA Low Level Term Version 4 Code (o) 6981808 AELLT4CD	The code representing the reported MedDRA version 4 low level term. CDASH: AELLTCD (6355777); SDTM: AELLTCD (No CDE)	CHARACTER. Use choice list.
Adverse Event Attribution to Product or Procedure Scale (o) 6981809 AEABTXSC	The degree of certainty the adverse event is related to the agent or device. CDASH: AEREL (6338454); SDTM: AEREL (No CDE)	CHARACTER. Use choice list.
Adverse Event Domain Adverse Event Evaluation Interval End Date (o) 6981810 AERPENDT	The date of the final assessment of an adverse event represented in an unambiguous date format (e.g., DD-MON-YYYY). CDASH: No Match; SDTM: No Match	DATE

Field Name (Partition Status) CDE ID # Short Name	Definition CDISC Mapping and Instruction	Format
Adverse Event Last Clinical Trial Period Assessment Indicator (o) 6981824	The indication of whether or not the adverse event was assessed during the last clinical trial period.	CHARACTER. Use choice list.
AEASRTNY	CDASH: No Match; SDTM: No Match	
Expected Adverse Event Indicator (o) 6981825	The indication of whether or not the adverse event was expected.	CHARACTER. Use choice list.
AEEXPTNY	CDASH: No Match; SDTM: No Match	
Adverse Event Serious Event (o) 6343399 AESER	An indication whether or not the adverse event is determined to be "serious" based on what is defined in the protocol. CDASH: AESER (6343399);	CHARACTER. Use choice list.
	SDTM: AESER (No CDE)	
Start Time of Adverse Event (o) 6380821 AESTTIM	The start time of the adverse event represented in an unambiguous time format (e.g., hh:mm:ss).	CHARACTER
	CDASH: AESTTIM (6380821); SDTM: AESTDTC (No CDE)	
Clinical Trial Protocol Course Number (o) 6981826	The numeric representation of a single round of therapeutic treatment.	NUMBER
ECCORSEN	CDASH: No Match; SDTM: No Match	
Adverse Event Evaluation Interval Begin Date (o) 6981827 AERPSTDT	The date the clinical trial reporting period started represented in an unambiguous date format (e.g., DD-MON-YYYY).	DATE
	CDASH: No Match; SDTM: No Match	

Field Name (Partition Status) CDE ID # Short Name	Definition CDISC Mapping and Instruction	Format
Preexisting Condition Indicator (o) 6981835 AEPREXNY	The indication of whether or not the adverse event is a pre-existing condition. CDASH: No Match; SDTM: No	CHARACTER. Use choice list.
End Time of Adverse Event (o) 6380822 AEENTIM	Match The time when the adverse event ended/resolved represented in an unambiguous time format (e.g., hh:mm:ss). CDASH: AEENTIM (6380822); SDTM: AEENDTC (No CDE)	CHARACTER
Ongoing Adverse Event (o) 6343381 AEONGO	Indication AE is ongoing when no End Date is provided. CDASH: AEONGO (6343381); SDTM: If Yes, AEENRTPT (6619608) = 'ONGOING'	CHARACTER. Use choice list.
Outcome of Adverse Event (o) 6343392 AEOUT	A description of the outcome of an event. CDASH: AEOUT (6343392); SDTM: AEOUT (No CDE)	CHARACTER. Use choice list.
Adverse Event Pattern Type (o) 6981828 AEPTRNTP	The indication of the pattern of the adverse event over time. CDASH: AEPATT (6380058); SDTM: AEPATT (No CDE)	CHARACTER. Use choice list.
Adverse Event Post Protocol Agent Restart Recurrence Indicator (o) 6981829 AEREAPNY	The indication of whether or not the adverse event recurred after the protocol agent was restarted. CDASH: No Match; SDTM: No Match	CHARACTER. Use choice list.
Common Terminology Criteria for Adverse Events Comment Value Text (o) 7147754 AECOVAL	A free text field describing Common Terminology Criteria for Adverse Events comments. CDASH: COVAL (6355806); SDTM: No Match	CHARACTER

Field Name (Partition Status) CDE ID # Short Name	Definition CDISC Mapping and Instruction	Format
Serious Adverse Event Reason Code (o) 6981830 AESERURN	The code that describes the reason an adverse event is defined as serious. CDASH: No Match; SDTM: No Match	CHARACTER. Use choice list.
Serious Adverse Event Reason Text (o) 6981831 AESERRNX	The description of the reason an adverse event is defined as serious not previously listed. CDASH: No Match; SDTM: No Match	CHARACTER
Adverse Event Dose Restriction Indicator (o) 6981832 AEDSTXNY	The indication of whether or not the adverse event was dose- limiting. CDASH: No Match; SDTM: No Match	CHARACTER. Use choice list.

Annotated CRF: Adverse Event/Serious Adverse Event CTCAE v4.0 CDISC Aligned NCI Standard Template

This annotated CRF is ONLY used to show CDISC mapping without consideration of the CRF layout. CDASH mapping is in **Blue**, and SDTM mapping is in **Red**.

Form Name: Adverse Event/Serious Adverse Event CTCAE v4.0 CDISC Aligned NCI Standard Template

Mandatory Questions

CRF Question	Value Domain
Adverse Event Term (v4.0) (6981742) CDE Short Name: AELLT4NM	CHARACTER – Maximum Length = 84
	List of 790 PVs
CDASH: AELLT (6355960) Subset of Adverse Event MedDRA Low Level Term	
SDTM: AELLT (No CDE)	
Describe 'Other' Adverse Event (6338308) CDE Short Name: AETERM	CHARACTER – Maximum Length = 200
CDASH: AETERM (6338308)	
SDTM: AETERM (No CDE)	
Adverse Event Grade (6981800) CDE Short Name: AEAESVGD	ALPHANUMERIC – Maximum Length = 1
	☐ 0 – Absent Adverse Event
CDASH: AETOXGR (6338618)	☐ 1 – Mild Adverse Event
	☐ 2 – Moderate Adverse Event
SDTM: AETOXGR (No CDE)	☐ 3 – Severe Adverse Event
	☐ 4 – Life Threatening Adverse Event
	☐ 5 – Death Related to Adverse Event

Conditional Questions

CRF Question	Value Domain
AE Start Date (6341142) CDE Short Name: AESTDAT	DATE – Maximum Length = 11
CDASH: AESTDAT (6341142)	
SDTM: AESTDTC (No CDE)	
Was patient hospitalized for toxicity? (6343376)	CHARACTER – Maximum Length = 2
CDE Short Name: AESHOSP	□ N – No
CDASH: AESHOSP (6343376)	□ NA – Not Applicable□ U – Unknown□ Y – Yes
SDTM: AESHOSP (No CDE)	
Cycle # (6981801) CDE Short Name: ECTXCYNU	NUMBER – Maximum Length = 10
CDASH: No Match	
SDTM: No Match	

Optional Questions

CRI	- Question	Value Domain
	what is the AE attributed? (6981806) Short Name: AEATRBTP	CHARACTER – Maximum Length = 22
		☐ Biological Therapy – Biological Therapy
	CDASH: No Match	☐ Chemotherapy – Chemotherapy
		☐ Combined modality – combined modality
	SDTM: No Match	☐ Concomitant medication – Concomitant Agent
		☐ Device – Medical_Device
		☐ Disease – disease
		☐ Endocrine Therapy – Endocrine Therapy
		☐ Immunotherapy – Immunotherapy
		☐ Investigational agent – Investigational Agent
		☐ Other – Other
		☐ Radiation therapy – Radiation Therapy
		☐ Surgery – Surgery
Oth	er Attribution, Specify (6981833)	CHARACTER – Maximum Length = 200
CDE	E Short Name: AEATBTPX	
	CDASH: No Match	
	SDTM: No Match	
	Stop Date (6340298) E Short Name: AEENDAT	DATE – Maximum Length = 11
	CDASH: AEENDAT (6340298)	
	SDTM: AEENDTC (No CDE)	

MedDRA System Organ Class (SOC) (6981807)	СН	ARACTER – Maximum Length = 80
CDE Short Name: AEMSOCNM		Blood and lymphatic system disorders – Hematopoietic and Lymphoid System Disorder
CDASH: AESOC (6380294)		Cardiac disorders – Cardiac disorders
SDTM: AEBODSYS (6658533)		Congenital, familial and genetic disorders – Congenital, Familial and Genetic Disorder Class
		Ear and labyrinth disorders – Ear and Labyrinth Disorder Class
		Endocrine disorders – Endocrine Disorder
		Eye disorders – Eye Disorder
		Gastrointestinal disorders – Gastrointestinal Disorder
		General disorders and administration site conditions – General Disorders and Administration Site Conditions Class
		Hepatobiliary disorders – Liver and Biliary Tract Disorder
		Immune system disorders – Immune System Disorder
		Infections and infestations – Infection and infestation
		Injury, poisoning and procedural complications – Injury, Poisoning and Procedural Complication Class
		Investigations – Investigation
		Metabolism and nutrition disorders – Metabolism and Nutrition Disorder Class
		Musculoskeletal and connective tissue disorders – Connective and Soft Tissue Disorder
		Neoplasms benign, malignant and unspecified (incl cysts and polyps) – Neoplasm
		Nervous system disorders – Nervous System Disorder
		Pregnancy, puerperium and perinatal conditions – Pregnancy, Puerperium and Perinatal Condition Class
		Psychiatric disorders – Psychiatric Disorder
		Renal and urinary disorders – Urinary Tract Disorder
		Reproductive system and breast disorders – Reproductive System and Breast Disorder Class

CRF Question	Value Domain
	Respiratory, thoracic and mediastinal disorders – Respiratory and Thoracic Disorder
	Skin and subcutaneous tissue disorders – Skin Disorder
	☐ Social circumstances – Social Circumstances
	☐ Surgical and medical procedures – Intervention or Procedure
	☐ Vascular disorders – Vascular Disorder
MedDRA AE Code (CTCAE v4.0) (6981808) CDE Short Name: AELLT4CD	Character – Maximum Length = 8
	List of 790 PVs
CDASH: AELLTCD (6355777)	
SDTM: AELLTCD (No CDE)	
AE Attribution (6981809) CDE Short Name: AEABTXSC	CHARACTER – Maximum Length = 10
	☐ Definite – DEFINITE
CDASH: AEREL (6338454)	Possible – POSSIBLE
SDTM: AEREL (No CDE)	Probable – PROBABLE
OD TWI. ALIKEE (NO ODE)	Unlikely – UNLIKELY□ Unrelated – UNRELATED
Reporting Period End Date (6981810) CDE Short Name: AERPENDT	DATE – Maximum Length = 11
CDASH: No Match	
SDTM: No Match	
Were adverse events assessed during most recent period (6981824)	CHARACTER – Maximum Length = 2
CDE Short Name: AEASRTNY	
	N – No
CDASH: No Match	□ NA – Not Applicable□ U – Unknown
SDTM: No Match	☐ Y – Yes

CRF Question	Value Domain
Expected? (Yes/No) (6981825) CDE Short Name: AEEXPTNY	CHARACTER – Maximum Length = 2
CDASH: No Match SDTM: No Match	 N − No NA − Not Applicable U − Unknown Y − Yes
Serious? (6343399) CDE Short Name: AESER	CHARACTER – Maximum Length = 2 □ N – No
CDASH: AESER (6343399)	□ NA – Not Applicable □ U – Unknown
SDTM: AESER (No CDE)	☐ Y – Yes
Event Onset Time (6380821) CDE Short Name: AESTTIM CDASH: AESTTIM (6380821)	CHARACTER – Maximum Length = 8
SDTM: AESTDTC (No CDE)	
Course (6981826) CDE Short Name: ECCORSEN	NUMBER – Maximum Length = 10
CDASH: No Match	
SDTM: No Match	
AE Evaluation Period Start Date (6981827) CDE Short Name: AERPSTDT	DATE – Maximum Length = 11
CDASH: No Match	
SDTM: No Match	
Pre-existing AE? (6981835) CDE Short Name: AEPREXNY	CHARACTER – Maximum Length = 2
CDASH: No Match	□ NA – Not Applicable □ U – Unknown
SDTM: No Match	☐ Y – Yes

CRF Question	Value Domain
AE Resolved Time (6380822) CDE Short Name: AEENTIM	CHARACTER – Maximum Length = 8
CDASH: AEENTIM (6380822);	
SDTM: AEENDTC (No CDE)	
Is the adverse event ongoing? (6343381) CDE Short Name: AEONGO	CHARACTER – Maximum Length = 2
CDASH: AEONGO (6343381)	□ N – No□ NA – Not Applicable□ U – Unknown
SDTM: If Yes, AEENRTPT (6619608) = 'ONGOING'	☐ Y – Yes
Participant Status/Outcome (6343392) CDE Short Name: AEOUT	CHARACTER – Maximum Length = 100
CDASH: AEOUT (6343392)	 □ FATAL – Death Related to Adverse Event □ NOT RECOVERED/NOT RESOLVED – Not Recovered or Not Resolved
SDTM: AEOUT (No CDE)	☐ RECOVERED/RESOLVED – Recovered or Resolved PV – PVM
	RECOVERED/RESOLVED WITH SEQUELAE – Recovered/Resolved with Sequelae
	RECOVERING/RESOLVING – Recovering or Resolving
	UNKNOWN – Unknown
Adverse Event Condition Pattern (6981828) CDE Short Name: AEPTRNTP	CHARACTER – Maximum Length = 1
	☐ 1 – Single Episode
CDASH: AEPATT (6380058)	2 – Intermittent
SDTM: AEPATT (No CDE)	3 – Continuous
Did event reappear after study agent was reintroduced? (6981829)	CHARACTER – Maximum Length = 2
CDE Short Name: AEREAPNY	□ N – No
CDASH: No Match	□ NA – Not Applicable□ U – Unknown
	□ Y – Yes
SDTM: No Match	

CRF Question	Value Domain
Comments (7147754) CDE Short Name: AECOVAL	CHARACTER – Maximum Length = 200
CDASH: COVAL (6355806)	
SDTM: No Match	
Why serious? (6981830) CDE Short Name: AESERURN	CHARACTER – Maximum Length = 1
ODAGU N. M. J.	1 – Results in Death
CDASH: No Match	2 – Is life-threatening
SDTM: No Match	☐ 3 – Requires inpatient hospitalization or prolongation of existing hospitalization
	 4 – Results in persistent or significant disability/incapacity
	☐ 5 – Is a congenital anomaly/birth defect
	 6 – In the medical judgment of the treating physician and/or investigator, it may jeopardize the participant or require intervention to prevent one of these outcomes
	☐ 7 – Other specify
	8 – Meets criteria per protocol but does not meet other criterion (above)
Other, specify (6981831) CDE Short Name: AESERRNX	CHARACTER – Maximum Length = 200
CDASH: No Match	
SDTM: No Match	
Dose-Limiting Toxicity? (6981832)	CHARACTER – Maximum Length = 2
CDE Short Name: AEDSTXNY	
22.20.00	☐ N – No
CDASH: No Match	☐ NA – Not Applicable
ODTIV N. M. C.	U – Unknown
SDTM: No Match	☐ Y – Yes