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 v5.0 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 v5.0 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 5 Name (m) 6981836 AELLT5NM	The name of the reported MedDRA version 5 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). 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.	DATE
Initial or Prolonged Hospitalization (c) 6343376 AESHOSP	An indication the serious adverse event resulted in an initial or prolonged hospitalization. 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.	CHARACTER. Use choice list.
Therapeutic Procedure Cycle Number (c) 6981801 ECTXCYNU	The numeric representation of a round of therapeutic treatment that may contain more than one cycle. CDASH: No Match; SDTM: No Match; Conditionality Rule: Studies use cycles.	NUMBER
Therapeutic Procedure Or Disease or Disorder Attribution Type (o) 6981806 AEATRBTP	The treatment modality or disease associated as a cause of the event. CDASH: No Match; SDTM: No Match	CHARACTER. Use choice list.

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 Code Version 5 Code (o) 6981834 AELLT5CD	The name of the reported MedDRA version 5 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 AEASRTNY	The indication of whether or not the adverse event was assessed during the last clinical trial period. CDASH: No Match; SDTM: No Match	CHARACTER. Use choice list.
Expected Adverse Event Indicator (o) 6981825 AEEXPTNY	The indication of whether or not the adverse event was expected. CDASH: No Match; SDTM: No Match	CHARACTER. Use choice list.
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); SDTM: AESER (No CDE)	CHARACTER. Use choice list.
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). CDASH: AESTTIM (6380821); SDTM: AESTDTC (No CDE)	CHARACTER
Clinical Trial Protocol Course Number (o) 6981826 ECCORSEN	The numeric representation of a single round of therapeutic treatment. CDASH: No Match; SDTM: No Match	NUMBER
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). CDASH: No Match; SDTM: No Match	DATE

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 Match	CHARACTER. Use choice list.
End Time of Adverse Event (o) 6380822 AEENTIM	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 v5.0 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 v5.0 CDISC Aligned NCI Standard Template

Mandatory Questions

CRF Question	Value Domain
Adverse Event Term (v5.0) (6981836) **CDE Short Name:** AELLT5NM CDASH: AELLT (6355960) Subset of Adverse Event MedDRA Low Level Term SDTM: AELLT (No CDE)	CHARACTER – Maximum Length = 100 List of 837 PVs
Describe 'Other' Adverse Event (6338308) **CDE Short Name:** AETERM CDASH: AETERM (6338308) SDTM: AETERM (No CDE)	CHARACTER – Maximum Length = 200
Adverse Event Grade (6981800) **CDE Short Name:** AEAESVGD CDASH: AETOXGR (6338618) SDTM: AETOXGR (No CDE)	ALPHANUMERIC – Maximum Length = 1 ☐ 0 – Absent Adverse Event ☐ 1 – Mild Adverse Event ☐ 2 – Moderate Adverse Event ☐ 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 CDASH: AESTDAT (6341142) SDTM: AESTDTC (No CDE)	DATE – Maximum Length = 11
Was patient hospitalized for toxicity? (6343376) **CDE Short Name:** AESHOSP CDASH: AESHOSP (6343376) SDTM: AESHOSP (No CDE)	CHARACTER – Maximum Length = 2 ☐ N – No ☐ NA – Not Applicable ☐ U – Unknown ☐ Y – Yes
Cycle # (6981801) **CDE Short Name:** ECTXCYNU CDASH: No Match SDTM: No Match	NUMBER – Maximum Length = 10

Optional Questions

CRF Question	Value Domain
To what is the AE attributed? (6981806) **CDE Short Name:** AEATRBTP CDASH: No Match SDTM: No Match	CHARACTER – Maximum Length = 22 ☐ Biological Therapy – Biological Therapy ☐ Chemotherapy – Chemotherapy ☐ Combined modality – combined modality ☐ 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
Other Attribution, Specify (6981833) **CDE Short Name:** AEATBTPX CDASH: No Match SDTM: No Match	CHARACTER – Maximum Length = 200
AE Stop Date (6340298) **CDE Short Name:** AEENDAT CDASH: AEENDAT (6340298) SDTM: AEENDTC (No CDE)	DATE – Maximum Length = 11

MedDRA System Organ Class (SOC) (6981807) **CDE Short Name:** AEMSOCNM CDASH: AESOC (6380294) SDTM: AEBODSYS (6658533)	CHARACTER – Maximum Length = 80 ☐ Blood and lymphatic system disorders – Hematopoietic and Lymphoid System Disorder ☐ Cardiac disorders – Cardiac disorders ☐ 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 v5.0) (6981834) **CDE Short Name:** AELLT5CD CDASH: AELLTCD (6355777) SDTM: AELLTCD (No CDE)	Character – Maximum Length = 8 List of 837 PVs
AE Attribution (6981809) **CDE Short Name:** AEABTXSC CDASH: AEREL (6338454) SDTM: AEREL (No CDE)	CHARACTER – Maximum Length = 10 ☐ Definite – DEFINITE ☐ Possible – POSSIBLE ☐ Probable – PROBABLE ☐ Unlikely – UNLIKELY ☐ Unrelated – UNRELATED
Reporting Period End Date (6981810) **CDE Short Name:** AERPENDT CDASH: No Match SDTM: No Match	DATE – Maximum Length = 11
Were adverse events assessed during most recent period (6981824) **CDE Short Name:** AEASRTNY CDASH: No Match SDTM: No Match	CHARACTER – Maximum Length = 2 ☐ N – No ☐ NA – Not Applicable ☐ U – Unknown ☐ Y – Yes

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

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

CRF Question	Value Domain
Comments (7147754) **CDE Short Name:** AECOVAL CDASH: COVAL (6355806) SDTM: No Match	CHARACTER – Maximum Length = 200
Why serious? (6981830) **CDE Short Name:** AESERURN CDASH: No Match SDTM: No Match	CHARACTER – Maximum Length = 1 ☐ 1 – Results in Death ☐ 2 – Is life-threatening ☐ 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 CDASH: No Match SDTM: No Match	CHARACTER – Maximum Length = 200
Dose-Limiting Toxicity? (6981832) **CDE Short Name:** AEDSTXNY CDASH: No Match SDTM: No Match	CHARACTER – Maximum Length = 2 ☐ N – No ☐ NA – Not Applicable ☐ U – Unknown ☐ Y – Yes