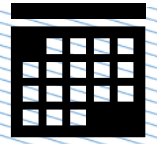
Define-XML v2.1 – what's new



14-Mar-2023

Steffen Müller

Regulatory support … and requirement

FDA Data Standards Catalog v9.0 (01/25/2023) - Submission Data Standards

For full description of column headings, see Instr.& Column Descriptions tab

Data Standard	Exchange Format	Standards Development Organization (SDO)	Version(s)	Designated Implementation Guide Version(s)	FDA Center(s)	Date Support Begins (MM/DD/YYYY)	Date Support Ends (MM/DD/YYYY)	Date Requirement Begins (MM/DD/YYYY) [10] [11]	Date Requirement Ends (MM/DD/YYYY)
Define	XML	CDISC	1	N/A	CDER, CBER	Ongoing	03.15.2018	12/17/2016 [1] 12/17/2017 [2]	03.15.2018
Define	XML	CDISC	2	N/A	CDER, CBER	08.07.2013		12/17/2016 [1] 12/17/2017 [2]	
Define	XML	CDISC	2,1	N/A	CDER, CBER	03.15.2021		03.15.2023	

Context and Applicable Standards

Date/Time of Define-XML document generation: 2019-02-11T15:30:01
Define-XML version: 2.1.0
def:Context
Define-XML Context: Submission
Stylesheet version: 2019-02-11

Study Name	CDISC01_1
Study Description	CDISC Test Study Modified to illustrate Define-XML 2.1 features
Protocol Name	CDISC01-1
Metadata Name	Study CDISC01_1, Data Definitions V-1
Metadata Description	Data Definitions for CDISC01-01 SDTM datasets.

Standards for Study CDISC01_1

Standard	Type	Status	Documentation
SDTMIG 3.1.2	IG	Final	The CDISC01 study was modeled on a very old SDTMIG and no attempt was done yet to upversion it to a newer SDTMIG
SDTMIG 3.2	IG	Final	As an example, the CDISC01 study was adjusted to include a new Domain available in SDTM IG 3.2
SDTMIG-MD 1.0	IG	Final	As an example, the CDISC01 study was adjusted to include a new Domain available in SDTMIG-MD 1.0. The XS Domain is expected to reference the device used with variable SPDEVID.
CDISC/NCI SDTM 2011-12-09	CT	Final	Assuming the CT was not upversioned for this study
CDISC/NCI SDTM 2015-12-18	CT	Final	The CT version applicable for the new Domain is the 2015-12-18 version

Dataset Metadata Referencing the Applicable Standard

Datasets

Dataset	Description	Class	Structure	Purpose
TS [SDTMIG 3.1.2]	Trial Summary	TRIAL DESIGN	One record per trial summary parameter value	Tabulation
DI [SDTMIG-MD 1.0]	Device Identifiers	SPECIAL PURPOSE	One record per device identifier per device	Tabulation
DM [SDTMIG 3.1.2]	Demographics	SPECIAL PURPOSE	One record per subject	Tabulation
EC [SDTMIG 3.2]	Exposure as Collected	INTERVENTIONS	One record per constant dosing interval per subject	Tabulation
XS [Non Standard]	S Findings	FINDINGS	One record per finding per visit per subject	Tabulation

CTs Referencing the Applicable Standards

Domain Abbreviation (DI) [*C66734*] [CDISC/NCI SDTM 2015-12-18]

Permitted Value (Code)	Display Value (Decode)
DI [*C102618*]	Device Identifiers

Domain Abbreviation (DM) [*C66734*] [CDISC/NCI SDTM 2011-12-09]

Permitted Value (Code)	Display Value (Decode)
DM [*C49572*]	Demographics

```
<CodeList OID="CL.DI.DOMAIN"
          Name="Domain Abbreviation (DI)"
          DataType="text"
          def:StandardOID="STD.4"
          SASFormatName="$DIDOMAI">
  <CodeListItem CodedValue="DI">
    <Decode>
      <TranslatedText xml:lang="en">Device Identifiers</TranslatedText>
    </Decode>
    <Alias Context="nci:ExtCodeID" Name="C102618"/>
  </CodeListItem>
  <Alias Context="nci:ExtCodeID" Name="C66734"/>
</CodeList>
<CodeList OID="CL.DM.DOMAIN"
          Name="Domain Abbreviation (DM)"
          DataType="text"
          def:StandardOID="STD.3"
```

New Information: SubClass

Datasets

Dataset	Description	Class - SubClass	Structure	Purpose	Keys	Documentation	Location
ADSL [ADaMIG 1.1]	Subject-Level Analysis	SUBJECT LEVEL ANALYSIS DATASET	one record per subject	Analysis	STUDYID, USUBJID	Screen Failures are excluded since they are not needed for this study analysis. See referenced dataset creation program and ADRG adsl.sas Analysis Data Reviewer's Guide [6]	adsl.xpt
ADQSADAS [ADaMIG 1.1]	ADAS-Cog Analysis	BASIC DATA STRUCTURE	One record per subject per parameter per analysis visit per analysis date	Analysis	STUDYID, USUBJID, PARAMCD, AVISIT, ADT	See referenced dataset creation program and ADRG adqsadas.sas Analysis Data Reviewer's Guide [Section2.1]	adqsadas.xpt
ADAE [ADaMIG 1.1]	Adverse Events Analysis Dataset	OCCURRENCE DATA STRUCTURE • ADVERSE EVENT	one record per subject per adverse event	Analysis	STUDYID, USUBJID, AETERM, ASTDT, AESEQ	See SAS program adae.sas	adae.xpt

```
<def:Class Name="OCCURRENCE DATA STRUCTURE">
    <def:SubClass Name="ADVERSE EVENT"/>
</def:Class>
```

New Information: SubClass

- Note: There is no requirement that a SubClass is defined for every ADaM dataset.
- Defined in
  - Define-XML Controlled Terminology
    - Dependent on "parent" Class
    - CTs may grow over time
  - ADaM documents (examples):
    - ADVERSE EVENT defined in OCCDS IG 1.1
    - For TIME-TO-EVENT CDISC ADaM BDS TTE analysis document available + ADaMIG 1.3

Side Tour: Define-XML CT

A	B	C	D	E	F	G	H
Code	Codelist Code	Codelist Extensible (Yes/No)	Codelist Name	CDISC Submission Value	CDISC Synonym(s)	CDISC Definition	NCI Preferred Term
C165635		No	ADaM Basic Data Structure Subclass	BDSSC	ADaM Basic Data Structure Subclass	Terminology relevant to the subclasses of the ADaM basic data structure.	CDISC Define-XML ADaM Basic Data Structure Subclass Terminology
C172452	C165635		ADaM Basic Data Structure Subclass	NON-COMPARTMENTAL ANALYSIS	NCA	A dataset containing data that is used for	Non-Compartmental Analysis Dataset
C189348	C165635		ADaM Basic Data Structure Subclass	POPULATION PHARMACOKINETIC ANALYSIS	PPK	A dataset containing data that is used for population pharmacokinetic analyses.	Population Pharmacokinetic Analysis Dataset
C165637	C165635		ADaM Basic Data Structure Subclass	TIME-TO-EVENT	TTE	A dataset containing data that is used for	Time-to-Event Dataset
C177903		No	ADaM Medical Device Basic Data Structure Subclass	MDBDSSC	ADaM Medical Device Basic Data Structure Subclass	Terminology relevant to the subclasses of the ADaM device level basic data structure.	CDISC Define-XML ADaM Medical Device Basic Data Structure Subclass Terminology
C177920	C177903		ADaM Medical Device Basic Data Structure Subclass	MEDICAL DEVICE TIME-TO-EVENT	MDTTE	A dataset containing data that is used for medical device Time-to-Event analyses.	Medical Device Time-to-Event Dataset
C176227		No	ADaM Occurrence Data Structure Subclass	OCCSC	ADaM Occurrence Data Structure Subclass	Terminology relevant to the subclasses of the ADaM occurrence data structure.	CDISC Define-XML ADaM Occurrence Data Structure Subclass Terminology
C176265	C176227		ADaM Occurrence Data Structure Subclass	ADVERSE EVENT	AE	A dataset containing data that is used for adverse event analyses.	Adverse Event Dataset
C170452		No	Standard Name	STDNAM	Standard Name	Terminology relevant to the name of the standard described in the Define-XML	CDISC Define-XML Standard Name Terminology
C170552	C170452		Standard Name	ADaMIG		The implementation guide for the Clinical Data Interchange Standards Consortium	ADaM Implementation Guide
C163415	C170452		Standard Name	CDISC/NCI	CDISC Controlled Terminology; Clinical Data Interchange Standards Consortium Controlled Terminology	A standard terminology developed and maintained by Clinical Data Interchange Standards Consortium (CDISC) and the	Clinical Data Interchange Standards Consortium Controlled Terminology
C170455	C170452		Standard Name	SDTMIG		The implementation guide for the Clinical Data Interchange Standards Consortium	SDTM Implementation Guide
C170553	C170452		Standard Name	SDTMIG-AP		The implementation guide for the Clinical Data Interchange Standards Consortium (CDISC) Study Data Tabulation Model	SDTM Implementation Guide-Associated Persons
C170554	C170452		Standard Name	SDTMIG-MD		The implementation guide for the Clinical Data Interchange Standards Consortium (CDISC) Study Data Tabulation Model	SDTM Implementation Guide-Medical Devices

https://www.cancer.gov/research/resources/terminology/cdisc#define-xml-terminology

Origin (Type) => Origin (Type + Source)

ADQSADAS (ADAS-Cog Analysis) - [ADaMIG 1.1] Location: adqsadas.xpt

Variable	Where Condition	Label / Description	Type	Length or Display Format	Controlled Terms or ISO Format	Origin / Source / Method / Comment
STUDYID		Study Identifier	text	12		Predecessor: ADSL.STUDYID
ADY		Analysis Relative Day	integer	3		Derived (Source: Sponsor) ADY = ADT - TRTSDT + 1, if ADT>=TRTSDT. ADY = ADT - TRTSDT, if ADT<TRTSDT.
ADT		Analysis Date	integer	date9.		Derived (Source: Sponsor) SAS date from QS.QSDTC
PARAM		Parameter	text	100	ADAS-Cog Parameter [15 Terms]	Assigned (Source: Sponsor)
PARAMCD		Parameter Code	text	8	ADAS-Cog Parameter Code [15 Terms]	Assigned (Source: Sponsor)

More complex for SDTM

SDTM Origin – Type and Source Combinations

Type	Source				Notes
	Subject	Investigator	Vendor	Sponsor	
Collected	ePro	CRF	Lab data, ECG	X	This term should be used for clinical data that were actually observed or recorded by a person or received from an instrument; it should not be used for data that have been interpreted, calculated, or derived from other information.
Derived	X	X	Lab data, ECG	SDTM	Derivation examples include calculations performed during data collection (e.g., --DY). Other derivation examples: calculations within ePRO (e.g., questionnaire section scores) and calculations within EDC (e.g., BMI, BSA).
Assigned	X	X	Adjudicator	SDTM	Examples of this include third-party attributions by an adjudicator, coded terms that are supplied as part of a coding process, and values that are set independently of any subject-related data values in order to complete SDTM fields such as DOMAIN and --TESTCD
Protocol	X	X	X	SDTM	An example would be VSPOS (Vital Signs Position), which could be specified in the protocol and be provided by other means (e.g. CRF, eDT).
Predecessor	X	X	X	X	Use when a value is an exact copy of another value in an SDTM dataset.

Attribute def:HasNoData (SDTM)

- Mark with def:HasNoData="Yes" and explain via a Comment if data are missing
  - Dataset

XX [Non Standard] **[No Data]**	X Findings	FINDINGS	One record per finding per visit per subject	Tabulation	STUDYID, USUBJID, XXTESTCD, XXDTC, VISITNUM	Special domain contingent on rare conditions observed.	

  - Variable

XSORRESU **[No Data]**	Original Units	text	20	Units for S Findings Results • "g/dL" = "g/dL" • "mg/dL" = "mg/dL"	Collected (Source: Vendor) Planned Numeric tests were not performed.

  - Value-level, e.g.,
    QNAM value for "Other specify" is not available in the respective SUPP dataset because option other has never been selected

Thank You!

Questions?

Contact Details

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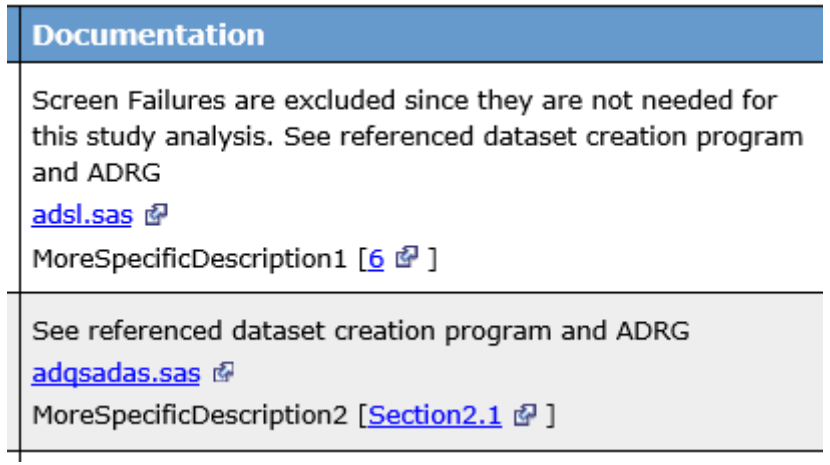
More efficient external document references

```
<def:CommentDef OID="COM.ADSL">
  <Description>
    <TranslatedText xml:lang="en">Screen Failures are excluded since they are not needed for this study analysis. See referenced dataset creation program and ADRG</TranslatedText>
  </Description>
  <def:DocumentRef leafID="LF.ADSL.PGM"/>
  <def:DocumentRef leafID="LF.ADRG">
    <def:PDFPageRef PageRefs="6" Type="PhysicalRef"  Title="MoreSpecificDescription1"/>
  </def:DocumentRef>
</def:CommentDef>
<def:CommentDef OID="COM.ADQSADAS">
  <Description>
    <TranslatedText xml:lang="en">See referenced dataset creation program and ADRG</TranslatedText>
  </Description>
  <def:DocumentRef leafID="LF.ADQSADAS.PGM"/>
  <def:DocumentRef leafID="LF.ADRG">
    <def:PDFPageRef PageRefs="Section2.1" Type="NamedDestination“ Title="MoreSpecificDescription2"/>
  </def:DocumentRef>
</def:CommentDef>
```



Compare respective documentation needs in Define-XML v2.0

```
<def:CommentDef OID="COM.ADSL">
  <Description>
   <TranslatedText>Screen Failures are excluded since they are not needed for this study analysis. See Analysis Data Reviewer's Guide, page 6.</TranslatedText>
  </Description>
  <def:DocumentRef leafID="LF.ADRG">
   <def:PDFPageRef PageRefs="6" Type="PhysicalRef"/>
  </def:DocumentRef>
 </def:CommentDef>
<def:CommentDef OID="COM.ADQSADAS">
  <Description>
   <TranslatedText>See referenced dataset creation program and Analysis Data Reviewer's Guide, Section 2.1</Translated
  </Description>
  <def:DocumentRef leafID="LF.ADQSADAS.PGM"/>
  <def:DocumentRef leafID="LF.ADRG">
   <def:PDFPageRef PageRefs="Section2.1" Type="NamedDestination"/>
  </def:DocumentRef>
 </def:CommentDef>
```

Documentation
Screen Failures are excluded since they are not needed for this study analysis. See Analysis Data Reviewer's Guide, page 6. Analysis Data Reviewer's Guide
See referenced dataset creation program and Analysis Data Reviewer's Guide, Section 2.1 adqsadas.sas Analysis Data Reviewer's Guide