



CDISC Italian User Network 2019

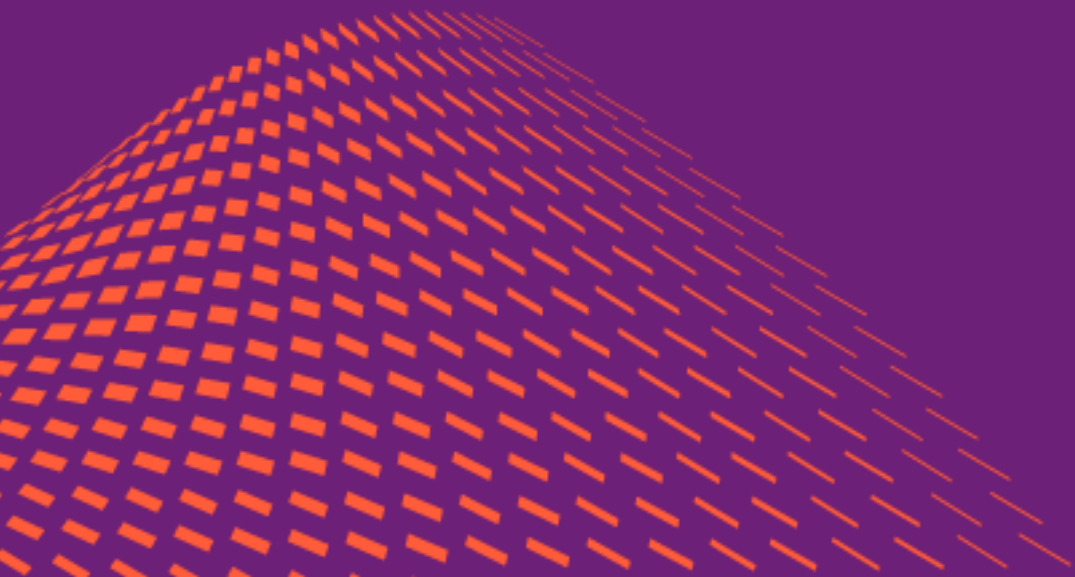
Milan, Italy | 22 February 2019

cdisc



Define-XML v2.1 CDISC guideline and PhUSE WG

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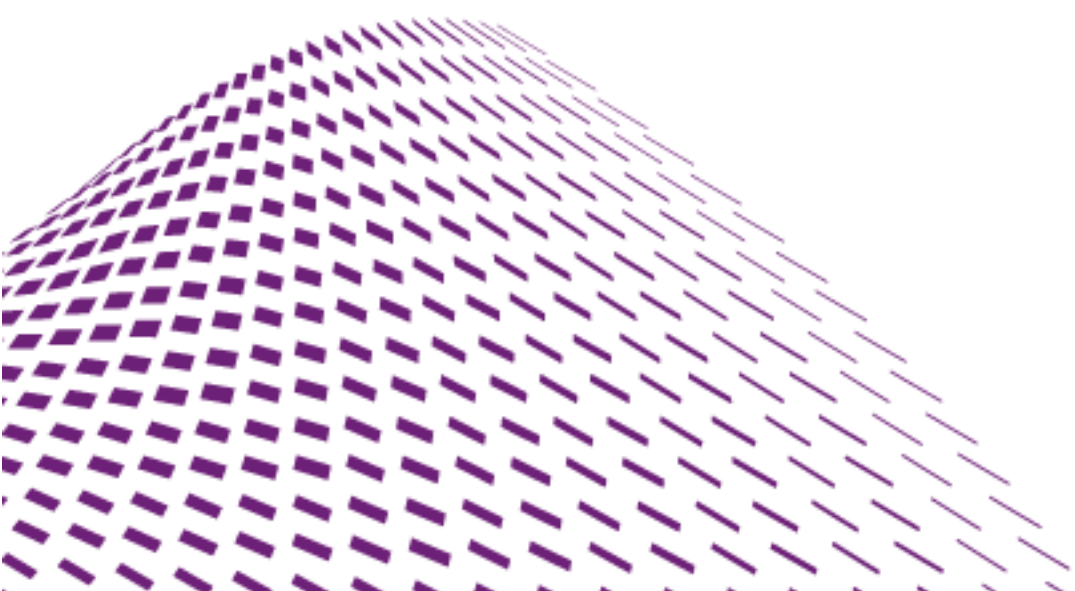


Agenda

1. Define-XML introduction
2. Define-XML v2.1
 - a. Changes
 - b. ARM integration
3. PhUSE Working Groups

Define-XML introduction

Contents, history, stylesheet



- Metadata are a **key component** for SDTM/ADaM/SEND datasets, they help to document, are stored into Define-XML.
- Define-xml is the document which provides the **fundamental components** of the metadata:
 - Datasets metadata
 - Variable metadata
 - Value-level metadata
 - Analysis Results Metadata (only for ADaM)
- Other define-XML components are:
 - Study metadata
 - Supporting documents metadata
 - Codelists

- **Define-XML v1.0** structure was different between SDTM and ADaM.
- **Define-XML v2.0** represents a significant update to Define-XML v1.0 in response to implementation experience with v1.0, the evolution of the SDTM/SEND/ADaM standards and best practice by SDTM/ADaM metadata experts. Key enhancement:
 - Support for CDISC Controlled Terminology
 - Flexible definition of Value Level Metadata
 - Enhanced documentation of data origin or source
 - Improved support for ADaM metadata
 - Improved handling of comments
- It is **good practice** to create define-XML before the related SDTM/SEND/ADaM datasets.
- Along with the proper Reviewer's Guide, Define-xml helps the reviewers to get into a submission package. Define-XML is the "**sponsor's truth**" about SDTM/SEND/ADaM content and structure. Define-XML is **mandatory** in submission to FDA and PMDA.

- Define-XML is not what you see **in the browser**, that is only a view on the define-xml, which is possible due to **stylesheet**.

Define-XML View

SDTM-IG 3.1.2

- Annotated Case Report Form
- Reviewers Guide
- Complex Algorithms
- ▶ Tabulation Datasets
- ▶ Value Level Metadata
- ▶ Controlled Terminology
- ▶ Computational Algorithms
- ▶ Comments

Date of document generation: 2013-03-03T17:04:44

Stylesheet version: 2013-04-24

Tabulation Datasets for Study CDISC01 (SDTM-IG 3.1.2)

Dataset	Description	Class	Structure	Purpose	Keys	Location	Documentation
TA	Trial Arms	TRIAL DESIGN	One record per planned Element per Arm	Tabulation	STUDYID, ARMCD, TAETORD	ta.xpt	
TE	Trial Elements	TRIAL DESIGN	One record per planned Element	Tabulation	STUDYID, ETCDD	te.xpt	
TI	Trial Inclusion/Exclusion Criteria	TRIAL DESIGN	One record per I/E criterion	Tabulation	STUDYID, IETESTCD	ti.xpt	
TS	Trial Summary	TRIAL DESIGN	One record per trial summary parameter value	Tabulation	STUDYID, TSPARMCD, TSSEQ	ts.xpt	
TV	Trial Visits	TRIAL DESIGN	One record per planned Visit per Arm	Tabulation	STUDYID, VISITNUM, ARMCD	tv.xpt	
DM	Demographics	SPECIAL PURPOSE	One record per subject	Tabulation	STUDYID, USUBJID	dm.xpt	See Reviewer's Guide, Section 2.1 Demographics Reviewers Guide

Define-XML Data

```
<!-- ***** -->
<!-- Value List Definitions Section (Required for Supplemental Qualifiers, Optional for other Normalized (Vertical) Datasets) -->
<!-- (Note that any definitions not provided at a Value Level will be inherited from the parent item definition) -->
<!-- ***** -->

<def:ValueListDef OID="VL.DA.DAORRES">
  <ItemRef ItemOID="IT.DA.DAORRES.DISPAMT" OrderNumber="1" Mandatory="Yes">
    <def:WhereClauseRef WhereClauseOID="WC.DA.DATESTCD.DISPAMT"/>
  </ItemRef>
  <ItemRef ItemOID="IT.DA.DAORRES.RETAMT" OrderNumber="2" Mandatory="No">
    <def:WhereClauseRef WhereClauseOID="WC.DA.DATESTCD.RETAMT"/>
  </ItemRef>
</def:ValueListDef>

<def:ValueListDef OID="VL.EG.EGORRES">
  <ItemRef ItemOID="IT.EG.EGORRES.INTP" OrderNumber="1" Mandatory="No">
    <def:WhereClauseRef WhereClauseOID="WC.EG.EGTESTCD.INTP"/>
  </ItemRef>
  <ItemRef ItemOID="IT.EG.EGORRES.PRMEAN" OrderNumber="2" Mandatory="No">
    <def:WhereClauseRef WhereClauseOID="WC.EG.EGTESTCD.PRMEAN"/>
  </ItemRef>
  <ItemRef ItemOID="IT.EG.EGORRES.QRSDUR" OrderNumber="3" Mandatory="No">
    <def:WhereClauseRef WhereClauseOID="WC.EG.EGTESTCD.QRSDUR"/>
  </ItemRef>
  <ItemRef ItemOID="IT.EG.EGORRES.QTMEAN" OrderNumber="4" Mandatory="No">
    <def:WhereClauseRef WhereClauseOID="WC.EG.EGTESTCD.QTMEAN"/>
  </ItemRef>
  <ItemRef ItemOID="IT.EG.EGORRES.VRMEAN" OrderNumber="5" Mandatory="No">
    <def:WhereClauseRef WhereClauseOID="WC.EG.EGTESTCD.VRMEAN"/>
  </ItemRef>
</def:ValueListDef>

<def:ValueListDef OID="VL.EG.EGSTRESC">
  <ItemRef ItemOID="IT.EG.EGSTRESC.QTCB" OrderNumber="1" Mandatory="Yes" MethodOID="MT.QTCB">
    <def:WhereClauseRef WhereClauseOID="WC.EG.EGTESTCD.QTCB"/>
  </ItemRef>
</def:ValueListDef>
```


- CDISC publishes default XSL stylesheets as part of the Define-XML packages:
 - 2005 Stylesheet for the Define-XML 1.0 standard
 - 2014 Stylesheet for the Define-XML 2.0 standard
 - 2015 Updated Define-XML 2.0 stylesheet with the additional support of Analysis Result Metadata representation, as part of the ARM 1.0 release
 - In 2016 a PhUSE working group was organized to develop a new version of the stylesheet. The upcoming updated Define-XML 2.0 stylesheet will also include the initial support for the draft Define-XML 2.1 standard
- All official CDISC stylesheets are available on the CDISC stylesheet library wiki page: <https://wiki.cdisc.org/display/PUB/Stylesheet+Library>.

Define-XML v2.1

Changes and ARM integration

- Currently Define-XML Specification v2.1 can be browsed from this link <https://wiki.cdisc.org/display/DEFXML2DOT1/Define-XML+2.1+Home>, which is in CDISC wiki and not on the CDISC website.
- The reason is that this document is **still a “draft”** and some work still needs to be done, then v2.1 is not an official release yet.
- For the same reason, the examples available with last **public review package** still need to be updated, then at the moment some new Elements and Attributes are available just through the examples present into the guideline.

Define-XML Code Examples

- [Illustration of Define-XML Document Structure](#)
- [Example Annotated CRF Reference](#)
- [Example MetaDataVersion Element](#)
- [Example of CDISC Controlled Terminology With an](#)
- [Example of CDISC Controlled Terminology Reference](#)
- [Example of a CodeList Using Rank Attribute](#)
- [Example of a CodeList With EnumeratedItem Element](#)
- [Example of a CodeList With Alias Elements for C-](#)
- [Example of a CodeList for External Dictionary Reference](#)
- [Example of ADaM Parameter-Level Metadata](#)

- Define-XML Sections - All sections of CDISC Define-XML Specification v2.1 can be browsed through the hyperlinked table of contents on the left.
- Define-XML Definition - contains the complete list of Define-XML Elements and Attributes present into CDISC Define-XML Specification v2.1.
- Define-XML Code Examples - contains the complete list of Define-XML Code Examples present into CDISC Define-XML Specification v2.1.

Define-XML v2.1 - Changes

This document includes changes to the Define-XML Version 2.0 specification that was published in 2013. The major changes between versions 2.0 and 2.1 are:

- **Versioning** of Standards and Controlled Terminology
 - Identifying sponsor define controlled terminology → *def:Standard@Type, def:Standard@Status, def:Standard/@PublishingSet*
 - Identifying non-standard domains or their version → *def:IsNonStandard / def:StandardOID*
 - Identifying non-standard variables → *def:IsNonStandard*
- Enhanced **Origin** information → *def:Origin/@Type, def:Origin/@Source*
- Enhanced **Document** references → *def:PDFPageRef/@Type, DocumentRef/@Title*
- Added **SubClass** → *ItemGroupDef/@def:Class def:SubClass*
- Added **HasNoData** → *def:HasNoData*
- Use of Alias for longer SAS names
- Context info can be added in the header e.g. *def:Context="Submission"*

Above in *italic* the **XML Schema enumerations** added for each purpose.

- **Versioning** of Standards and Controlled Terminology

Standards for Study CDISC Sample

Standard	Type	Status	Documentation
SDTMIG 3.2	IG	Final	The CDISC01 study was originally modeled on SDTM 3.1.2 but was updated when SDTM 3.2 was published.
SDTMIG-MD 1.0	IG	Final	Two domains from the SDTM Medical Devices Standard are included in this submission.
CDISC/NCI SDTM 2016-12-16	CT	Final	This CT version corresponds to the newest CT available in production at the time of preparing this example, just to illustrate best practices: 1) keeping the data and metadata as per the most current CT, if at all possible, 2) using only one CT version, if not allowed or agreed otherwise with the receiver of the data and metadata package. Reviewers should be aware that this is only an example and no attempt has been made to upversion the data to this CT version.

```
<def:Standards>
  <def:Standard OID="STD.SDTMIG-3.2" Name="SDTMIG" Type="IG" Version="3.2" Status="Final"
def:CommentOID="COM.STD2"/>
  <def:Standard OID="SDTM-MD-MDES 1.0" Name="SDTMIG-MD" Type="IG" Version="1.0" Status="Final"
def:CommentOID="COM.STD.MD"/>
  <def:Standard OID="STD.CT-2016-12-16" Name="CDISC/NCI" Type="CT" PublishingSet="SDTM"
Version="2016-12-16" Status="Final" def:CommentOID="COM.CT1"/>
</def:Standards>
```

Define-XML v2.1 - Changes

- Versioning of Standards and Controlled Terminology

Datasets

Dataset	Description	Class	Structure	Purpose	Keys	Documentation	Location
DM [SDTMIG 3.2]	Demographics	SPECIAL PURPOSE	One record per subject	Tabulation	STUDYID, USUBJID	See Reviewer's Guide, Section 2.1 Demographics Reviewers Guide [section2.1 @]	dm.xml @
EX [SDTMIG 3.2]	Exposure						
DS [SDTMIG 3.2]	Disposition		or protocol milestone per subject		DSSTDY, DSSTDTC, DSCAT, DSDECOD		
DI [SDTMIG-MD 1.0]	Device Identification						
DU [SDTMIG-MD 1.0]	Device Identification		test date per subject				
LB [SDTMIG 3.2]	Laboratory Test Results	FINDINGS	One record per analyte per visit per subject	Tabulation	STUDYID, USUBJID, LBCAT, LBMETHOD		lb.xml @
NS [Non Standard]	Non Standard Domain for Webinar Example	REFERENCE	REFID.				

```
<ItemGroupDef OID="IG.DM" Domain="DM" Name="DM" Repeating="No"
IsReferenceData="No" SASDatasetName="DM" Purpose="Tabulation"
def:Structure="One record per subject" def:CommentOID="COM.DOMAIN.DM"
def:StandardOID="STD.SDTMIG-3.2" def:ArchiveLocationID="LF.DM">
```

```
<ItemGroupDef OID="IG.MDES.DU.[SDTM]_MDES_1" Domain="DU" Name="DU" Purpose="Tabulation"
Repeating="Yes" def:StandardOID="SDTM-MD-MDES 1.0"
def:Structure="One record per property or setting per time point per visit or test date per subject"
def:ArchiveLocationID="LF.DU">
```

```
<ItemGroupDef OID="IG.NS.NS" Name="NS" Repeating="Yes" def:Structure="One definition per REFID."
Purpose="TABULATION" def:IsNonStandard="Yes" def:ArchiveLocationID="LF.NS">
```


- **Versioning** of Standards and Controlled Terminology

Type	Description	Allowable Names	Publishing Set
IG	<p>Implementation Guide that is based on a given CDISC Standard Model.</p> <p>The Model is implicit in the name of the IG. It is expected that the CDISC Standards Repository (SHARE) will describe the base model for each IG.</p>	SDTMIG SDTMIG-MD SDTMIG-AP SDTMIG-PGx SENDIG SENDIG-DART ADaMIG	
TAUG	<p>Therapeutic Area User Guide.</p> <p>It is assumed that TAUG standards are based on one or more IGs</p>	TAUG-Alzheimer's TAUG-Asthma TAUG-CHCV TAUG-Diabetes TAUG-Multiple Sclerosis TAUG-QT TAUG-XX	
CT	Controlled Terminology	CDISC/NCI	CDASH SDTM ADaM SEND

Define-XML v2.1 - Changes

- Versioning of Standards and Controlled Terminology

CDISC01-1

Annotated eCRF 

- Supplemental Documents
- Standards
- Datasets
- Controlled Terminology
- Methods

Expand all VLM

Collapse all VLM

Date/Time of Define-XML document generation: 2017-03-02T14:10:22

Define-XML version: 2.1.0

Define-XML Context: Submission

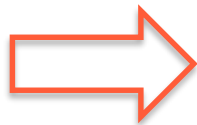
Stylesheet version: 2018-07-24 - Public Review

Study Name	CDISC01-1
Study Description	CDISC Test Study with minor modifications
Protocol Name	CDISC01
Metadata Name	Study CDISC01-1, Data Definitions, V-001
Metadata Description	Study CDISC01-1, Data Definitions, First Release using Define-XML 2.1(For Public Review)

This is a version of the metadata to highlight some of the main changes introduced in version 2.1 of the Define-XML Standard: - Versioning of Standards and Controlled Terminology - Identifying non-standard domains - Identifying non-standard variables - Enhanced Origin - Various (Context, additional Descriptions Comments, DocumentRef/@Title). Note that the metadata provided in this example file is not intended to be complete. Other explanation of the example may included in the Reviewers Guide and the corresponding section adjusted in the link below.

Reviewers Guide [\[section1.0 !\[\]\(e3275251d0893157c3584e20c81dc3ba_img.jpg\)](#)]

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 the new EC Domain and the new variable VSLAT available in the SDTMIG 3.2
CDISC/NCI SDTM 2016-12-16	CT	Final	This CT version corresponds to the newest CT available in production at the time of preparing this example, just to illustrate best practices: 1) keeping the data and metadata as per the most current CT, if at all possible, 2) using only one CT version, if not allowed or agreed otherwise with the receiver of the data and metadata package. Reviewers should be aware that this is only an example and no attempt has been made to upversion the data to this CT version.

Define-XML v2.1 - Changes

- **Versioning** of Standards and Controlled Terminology

Datasets

Dataset	Description	Class	Structure	Purpose	Keys	Documentation	Location
SC	Subject Characteristics	FINDINGS	One record per characteristic per subject	Tabulation	STUDYID, USUBJID, SCTESTCD		sc.xpt 
VS [SDTMIG 3.2]	Vital Signs	FINDINGS	One record per vital sign measurement per visit per subject	Tabulation	STUDYID, USUBJID, VSTESTCD, VSDTC, VISITNUM, VSPOS		vs.xpt 
XS [Non Standard]	S Findings	FINDINGS	One record per S finding per subject	Tabulation	STUDYID, USUBJID, XSTESTCD		xs.xpt 

Define-XML v2.1 - Changes

- Enhanced **Origin - Type and Source**, valid values for def:Origin/@Type, def:Origin/@Source

<i>Type</i>	Definition	<i>Source</i>			
		<i>Subject</i>	<i>Investigator</i>	<i>Vendor</i>	<i>Sponsor</i>
<i>Collected</i>	Data that were actually observed or recorded by a person or received from an instrument	ePro	CRF	Lab data, ECG	X
<i>Derived</i>	Data that is not directly collected, but is calculated by an algorithm or reproducible rule, which is dependent upon other data values.	X	X	Lab data, ECG	SDTM SEND ADaM
<i>Assigned</i>	Data that is determined by individual judgment as provided by an evaluator other than the subject or investigator.	X	X	X	SDTM SEND ADaM
<i>Protocol</i>	Data that is defined as part of the Trial Design preparation.	X	X	X	SDTM SEND
<i>Predecessor</i>	Data that is copied from a variable in another dataset.	X	X	X	SDTM ADaM

- Enhanced **Origin - Multiple Origin**
 - already supported in Define-XML v2.0 with the use of Value Level Metadata.
Example:
 - `Origin/@Type="CRF" when LBNAM EQ "VENDOR_A"`
 - `Origin/@Type="eDT" when LBNAM NE "VENDOR_A"`
 - this is still the best solution in Define-XML v2.1
 - However, in cases where there is no variable (like LBNAM) to differentiate, we **allow multiple def:Origin elements** for a variable.
 - A description should explain when each origin applies.
 - This should be a last resort solution, as there is no machine readable way to indicate when each origin is applicable.

Define-XML v2.1 - Changes

- Enhanced **Origin** – example

Content of Origin in Define-xml v2.0

Concomitant Medications (CM) [Location: [cm.xpt](#)]

Variable	Label	Key	Type	Length	Controlled Terms or Format	Origin	Derivation/Comment
STUDYID	Study Identifier	1	text	7		Protocol	
DOMAIN	Domain Abbreviation		text	2	["CM" = "Concomitant Meds"] < Domain Abbreviation (CM) >	Assigned	
USUBJID	Unique Subject Identifier	2	text	14		Derived	Concatenation of STUDYID and SUBJID
CMSEQ	Sequence Number		integer	2		Derived	Sequential number identifying records within each USUBJID in the domain.
CMTRT	Reported Name of Drug, Med, or Therapy	6	text	23		CRF Pages 9 22	
CMMODIFY	Modified Reported Name		text	23		Assigned	
CMDECOD	Standardized Medication Name		text	30	Drug Dictionary	Assigned	
CMCAT	Category for Medication	5	text	36	["CONCOMITANT MEDICATIONS", "PSYCHOTROPIC DRUG TREATMENT HISTORY"] < Category for Medication >	CRF Pages 9 22	

Define-XML v2.1 - Changes

- Enhanced **Origin** – example
Content of Origin in Define-xml v2.1

CM (Concomitant Medications) - INTERVENTIONS

Location: [cm.xpt](#)

Related Supplemental Qualifiers Dataset: [SUPPCM](#) (Supplemental Qualifiers for CM)

Variable	Label / Description	Type	Length or Display Format	Controlled Terms or ISO Format	Origin / Source / Method / Comment
CMCLAS	Medication Class	text	45	Drug Dictionary WHODRUG 200204	Assigned (Source: Sponsor) Coded to ATC level 3 Term based on CMINDC
CMCLASCD	Medication Class Code	text	3	Drug Dictionary WHODRUG 200204	Assigned (Source: Sponsor) Coded to ATC level 3 Code based on CMINDC
CMDOSTXT	Dose Description	text	4		Collected (Source: Investigator) Annotated eCRF [9 22]
CMDOSU	Dose Units	text	6	Unit (CM) [13 Terms]	Collected (Source: Investigator) Annotated eCRF [9 22]
CMDOSFRQ	Dosing Frequency per Interval	text	5	Frequency [9 Terms]	Collected (Source: Investigator) Annotated eCRF [22]

- An **optional** `def:DocumentRef/def:PDFPageRef/@Title` attribute was added. This title can be a more specific reference to a page or named destination than the generic document title that is defined by the `def:leaf/def:title` element. This **avoids proliferation of def:leaf elements**.

```
<!-- Leafs Definitions Section      -->
<def:leaf ID="LF.Table-14-3.01"
  xlink:href=" ../dummy-csr/dummy-csr.pdf">
  <def:title>Table 14-3.01 </def:title>
</def:leaf>
<def:leaf ID="LF.Table-14-5.02"
  xlink:href=" ../dummy-csr/dummy-csr.pdf">
  <def:title>Table 14-5.02 </def:title>
</def:leaf>
<def:leaf ID="LF.SAP-SEC-10.1.1"
  xlink:href=" ../dummy-csr/dummy-csr.pdf">
  <def:title>SAP Section 10.1.1</def:title>
</def:leaf>
<def:leaf ID="LF.SAP-SEC-11.2"
  xlink:href=" ../dummy-csr/dummy-csr.pdf">
  <def:title>SAP Section 11.2</def:title>
</def:leaf>
```

In Define-xml v2.0
proliferation of def:leaf

Define-XML v2.1 - Changes

- An **optional** `def:DocumentRef/def:PDFPageRef/@Title` attribute was added.
This title can be a more specific reference to a page or named destination than the generic document title that is defined by the `def:leaf/def:title` element.
This **avoids proliferation of `def:leaf` elements.**

```
<def:DocumentRef leafID="LF.CSR">  
  <def:PDFPageRef PageRefs="2" Type="PhysicalRef" Title="Table 14-3.01"/>  
</def:DocumentRef>
```

```
<def:DocumentRef leafID="LF.CSR">  
  <def:PDFPageRef PageRefs="5" Type="PhysicalRef" Title="Table 14-3.05"/>  
</def:DocumentRef>
```

```
<def:leaf ID="LF.CSR" xlink:href="../../dummy-csr/dummy-csr.pdf">  
  <def:title>Clinical Study Report</def:title>  
</def:leaf>
```

Code in `define-XML v2.1`

Define-XML v2.1 - Changes

- Added **SubClass** – Background
 - There was no way to identify specific applications of BDS and OCCDS classes, e.g. BDS dataset for time-to-event analysis
e.g. OCCDS dataset for adverse event analysis
 - SubClasses concept adhere to the definition of the parent Class but have additional requirements and rules to be considered.
 - The dataset **Class** attribute has been **re-implemented as a child element** with support for definition of Subclass.

```
<ItemGroupDef OID="IG.ADAE" Name="ADAE" SASDatasetName="ADAE"
  Repeating="Yes" IsReferenceData="No" Purpose="Analysis"
  def:Structure="one record per subject per adverse event"
  def:ArchiveLocationID="LF.ADAE">
  <Description>
    <TranslatedText xml:lang="en">Adverse Events Analysis Dataset</TranslatedText>
  </Description>
  <ItemRef ItemOID="IT.ADAE.STUDYID" OrderNumber="1" Mandatory="No" KeySequence="1"/>
  ...
  <ItemRef ItemOID="IT.ADAE.AOCC01FL" OrderNumber="55" Mandatory="No" />
  <def:Class Name="OCCURRENCE DATA STRUCTURE">
    <def:SubClass Name="ADVERSE EVENT"/>
  </def:Class>
  <def:leaf ID="LF.ADAE" xlink:href="adae.xpt">
    <def:title>adae.xpt </def:title>
  </def:leaf>
</ItemGroupDef>
```

Define-XML v2.1 - Changes

- Added **HasNoData**
 - Included in study definition, but not present in data
 - For ItemRef (variable case), required/expected/permissible (planned as part of study collection) in the context of a regulatory submission, as referenced in SDTM-IG v3.3 section 4.1.5 SDTM Core Designations
 - For ItemGroupDef (dataset case) is optional
- Use of **Alias for longer SAS names**
 - Where the Define-XML standard is used to transport dataset metadata of a legacy study in which the data format is in Dataset-XML.
- A **def:Context** attribute has been added to the ODM root element to indicate that Define-XML is for a regulatory submission.

Date/Time of Define-XML document generation: 2017-03-02T14:10:22

Define-XML version: 2.1.0

Define-XML Context: Submission

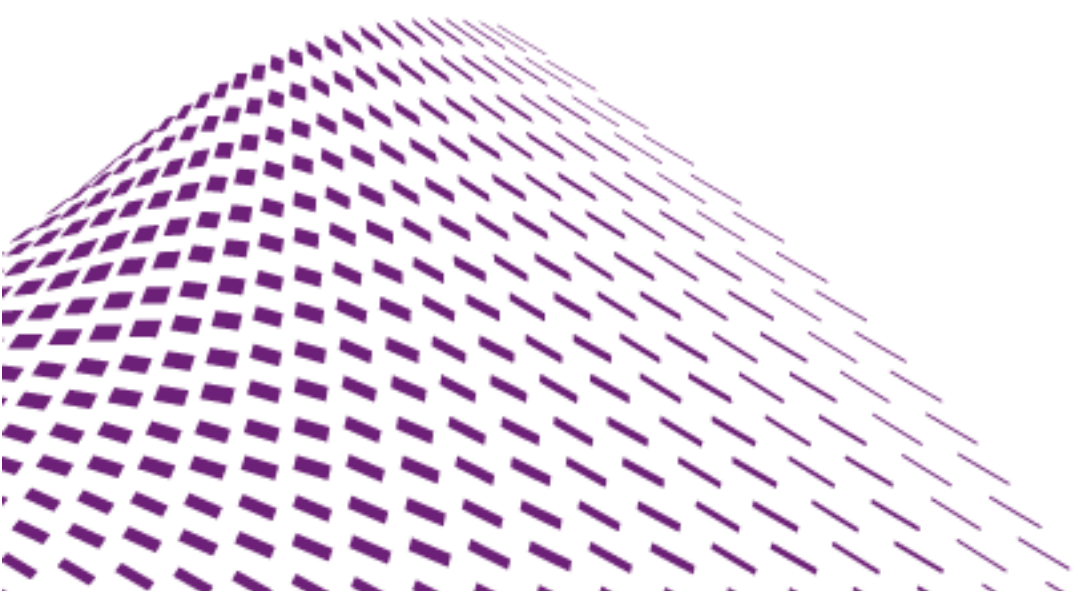
Stylesheet version: 2018-07-24 - Public Review

Study Name	CDISC01-1
Study Description	CDISC Test Study with minor modifications
Protocol Name	CDISC01
Metadata Name	Study CDISC01-1, Data Definitions, V-001
Metadata Description	Study CDISC01-1, Data Definitions, First Release using Define-XML 2.1(For Public Review)

- In Define-XML-2-0-Specification no reference to Analysis Results Metadata (ARM) extension was present. In Define-XML-2-1-Specification, **ARM extension** references have been **integrated**.
 - Section 3.3 Define-XML Document Structure
 - “Appendix A XML Schema” explains how the original XML Schema files that were part of the Analysis Results Metadata Standard extension to Define-XML version 2.0 can be updated to work with Define-XML version 2.1.
- Current guideline “Analysis Results Metadata v1.0 for Define-XML v2”
- In development **“Analysis Results Metadata (ARM) Validation Rules”**
 - Developing ARM validation rules to be used for define-xml compliance checks
 - Draft discussed within ADaM metadata subteam
 - Harmonization with CDISC Define-XML validation rules specifications ongoing
 - Final document should be published in 2019

PhUSE Working Groups

Optimizing Data Standards



- On PhUSE website, go to the Working Groups section and select Optimizing Data Standards
- For “Define-XML v2.0 Completion Guidelines & Stylesheet Recommendations” project the following outputs have been drafted:
 - **Completion Guidelines** draft document in <https://www.phuse.eu/cs-deliverables-under-review> - issued on Nov2018;
 - **Stylesheet Recommendations Public Review Package** downloadable from working group PhUSEwiki page - issued on Aug2018.
- Once finalized a document can be found in the White Paper section <https://www.phuse.eu/white-papers>.

- **Purpose and structure**

The purpose is **not to rephrase** the information contained in either the Define-XML 2.0 Specification or model implementation guides.

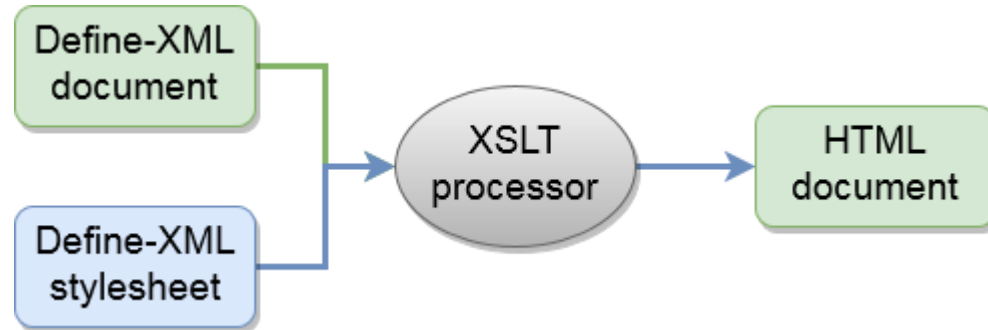
Under each section titled "Components of [xyz] Metadata", where [xyz] refers to each high-level metadata component, only the metadata items for which **clarifications, examples or guidelines** were considered to be added are included.

Even if the referenced standard in the title is Define-XML 2.0, the draft Define-XML 2.1 Standard content was also considered writing the guideline.

- **Useful tips** can be found in the following sections:

- Section 2.3 Dataset level
- Section 2.5 Value-level Metadata → **compatibility** from variable-level to value-level characteristics works in a single way direction.
- Section 2.6.3 General Considerations for Codelist → how to handle **extended** codelists, **enumerated and decoded** codelists, codelist **subsets**.

- **Stylesheet usage**



- The **rendered** version:

- gives a human-readable representation of metadata stored in a Define-XML document;
- does not show all of the information kept in it (e.g. the OID attribute which is used to connect Define-XML elements is not generally shown);
- does not use the same structure as it is defined in the Define-XML standard (e.g. Define-XML elements are ordered in accordance with the OrderNumber attribute where it is present. In other cases, the elements are ordered as they appear in the file).

- **Parameters:**

- for the Define-XML document development purposes, the stylesheet implements five parameters which can be set in an XSLT processor.

- Stylesheet Parameters

- **nCodeListItemDisplay** – default value [5]

The number of codelist items which is displayed in the "Controlled Terms or Format" column of the dataset view is controlled by the nCodeListItemDisplay parameter.

RACE	Race	text	40	Race [7 Terms]
ETHNIC	Ethnicity	text	22	Ethnic Group <ul style="list-style-type: none">• "HISPANIC OR LATINO"• "NOT HISPANIC OR LATINO"

- **displayMethodsTable** (0/1) – default value [1]

By default all algorithms are shown in a separate Methods table, which includes all of the methods described in the Define-XML document. This parameter allows to control whether this table is displayed or not.

– **displayCommentsTable** (0/1) – default value [0]

By default comments are not shown in a separate Comments table, which includes all comments described in the Define-XML document. This parameter allows to control whether this table is displayed or not. *e.g. see “Comment” in the ToC on the left.*



CDISC-Sample

- ▶ Supplemental Documents
- ▶ Datasets
- ▶ Controlled Terminology
- ▶ Methods
- ▶ Comments

Expand all VLM

Collapse all VLM

Comments

CommentOID	Description
COM.ADSL	Screen Failures are excluded since they are not needed for this study analysis
COM.ADQSADAS	See referenced dataset creation program and Analysis Data Reviewer's Guide, Section 2.1 adqsadas.sas  Analysis Data Reviewer's Guide [Section2.1 
COM.ADQSADAS.AVISITN	Numeric code for AVISIT
COM.ADQSADAS.PARAMN	Assign a numeric code for each value of PARAMCD (see codelist PARAMN_ADQSADAS)
COM.ADQSADAS.AWRANGE	Window range, specified in the SAP.
COM.ADQSADAS.AWTARGET	Target day within the window, specified in the SAP.
COM.ADQSADAS.AWLO	Start day of the window, specified in the SAP.
COM.ADQSADAS.AWHI	End day of the window, specified in the SAP.
COM.ADQSADAS.AWU	Assigned as "DAYS".
COM.ADSL.TRT01PN	Numeric code for TRT01P which corresponds to the randomized dose

– **displayPrefix** (0/1) – default value [0]

The "Origin/Source/Method/Comment" column combines different Define-XML attributes and elements. By setting this parameter to 1, prefixes [Comment], [Method], [Origin] will be displayed alongside with the descriptions, allowing to identify where it came from. *e.g. compare "Origin / Source / Method / Comment" column for ADSL dataset.*

ADSL (Subject-Level Analysis) - SUBJECT LEVEL ANALYSIS DATASET

Location: [adsl.xpt](#)

Variable	Label / Description	Type	Length [SignificantDigits] : Display Format	Controlled Terms or ISO Format	Origin / Source / Method / Comment
TRT01AN	Actual Treatment for Period 01 (N)	integer	8	ARMN <ul style="list-style-type: none"> • 0 = "Placebo" • 54 = "Xanomeline Low Dose" • 81 = "Xanomeline High Dose" 	[Origin] Assigned [Comment] Numeric code for TRT01A which corresponds to the randomized dose
TRTSDT	Date of First Exposure to Treatment	integer	8 : date9.		[Origin] Derived [Method]SV.SVSTDTC when SV.VISITNUM=3, converted to SAS date
TRTEDT	Date of Last Exposure to Treatment	integer	8 : date9.		[Origin] Derived [Method]The date of final dose (from the CRF) is EX.EXENDTC on the subject's last EX record. If the date of final dose is missing for the subject and the subject discontinued after visit 3, use the date of discontinuation as the date of last dose. Convert the date to a SAS date.

– **displayLengthDFormatSD** (0/1) – default value [0]

When there is a format attribute provided, it will be shown in the "Length or Display Format" column, otherwise only the length will be shown in this column. When this parameter is set to 1, name of the column will be changed to "Length [SignificantDigits] : Display Format" and all of the corresponding attributes, when present in the Define-XML document, will be shown in this column. *e.g. compare Length column for SDTM EG.*

EG (ECG Test Results) - FINDINGS

Related Supplemental Qualifiers Dataset: SUPPEG (Supplemental Qualifiers for EG)					
Variable	Where Condition	Label / Description	Type	Length or Display Format	Supplemental Qualifiers for EG
					Length [SignificantDigits] : Display Format
EGSTRESC VLM		Character Result/Finding in Std Format	text	15	15
	EGTESTCD = "QTCB" (QTcB - Bazett's Correction Formula)	QTcB - Bazett's Correction Formula	float	5.1	5 [1] : 5.1
	EGTESTCD = "QTCF" (QTcF - Fridericia's Correction Formula)	QTcF - Fridericia's Correction Formula	float	5.1	5 [1] : 5.1

- **Dataset Details**

- For each dataset, a separate table is created with the list of all variables and their details. For datasets with **Value-level metadata** (VLM) defined for at least one of its variables, both Variable- and Value-Level Metadata is shown in this table.

VLM presence: additional "Where Condition" column, 'VLM' in superscript next to variable name, collapse/expand option.

- **Supplemental qualifiers** vertical structure is expected to be described using a value-level metadata, but the layout is slightly different, e.g. no separate Where Clause column.
- **ISO8601** format is added only by the stylesheet, based on the data type of the variable.

PhUSE WG – Define-XML v2.0 Stylesheet Recommendations

- Dataset Details Value-level metadata *e.g. ADQSADAS*

Expand all VLM

Collapse all VLM

DTYPE VLM		Derivation Type	text	7	Derivation Type • "LOCF" = "Last Observation Carried Forward"	
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Expand all VLM

Collapse all VLM

DTYPE VLM		Derivation Type	text	7	Derivation Type • "LOCF" = "Last Observation Carried Forward"	
	PARAMCD NOT IN ("ACTOT" (Adas-Cog(11) Subscore))	Derivation Type	text	10	Derivation Type • "LOCF" = "Last Observation Carried Forward"	Assigned Value: null
	PARAMCD = "ACTOT" (Adas-Cog(11) Subscore)	Derivation Type	text	10	Derivation Type • "LOCF" = "Last Observation Carried Forward"	Assigned Value: LOCF denotes that the LOCF imputation method was used to impute the value for the given parameter and analysis visit.

PhUSE WG – Define-XML v2.0 Stylesheet Recommendations

- Dataset Details **Supplemental Qualifier e.g. SUPPAE**

QNAM	Qualifier variable name	text		7		Assigned
QLABEL	Qualifier Variable Label	text		30		Assigned
QVAL VLM	Data Value	text		60		

QLABEL	Qualifier Variable Label	text		30		Assigned
QVAL VLM	Data Value	text		60		
<ul style="list-style-type: none"> ▶ QNAM = "AETRTEM" 	Treatment Emergent Flag	text		1	No Yes Response Subset <ul style="list-style-type: none"> • "N" = "No" • "U" = "Unknown" • "Y" = "Yes" 	Derived AETRTEM = "Y" if Adverse Event was not present prior to the RFSTDTC, or it was present prior to the RFSTDTC but increased in severity during the treatment period. Null otherwise.
<ul style="list-style-type: none"> ▶ QNAM = "HLGT" 	High Level Group Term	text		52	Adverse Event Dictionary MEDDRA 8.0	Assigned
<ul style="list-style-type: none"> ▶ QNAM = "HLT" 	High Level Term	text		60	Adverse Event Dictionary MEDDRA 8.0	Assigned
<ul style="list-style-type: none"> ▶ QNAM = "LLT" 	Lowest Level Term	text		18	Adverse Event Dictionary MEDDRA 8.0	Assigned

Expand all VLM

Collapse all VLM

Expand all VLM

Collapse all VLM



Any question?

Thank You

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