

Define-XML v2: What's New?

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Agenda

- Define-XML History and Background
- What is Define-XML?
- Issues with Define-XML 1.0
- What's new in Define-XML 2.0?
- Displaying Define-XML (*stylesheet*)
- Next steps
- Questions

DEFINE-XML – HISTORY AND BACKGROUND



Define-XML HISTORY AND BACKGROUND

- **July 2004** - FDA adds Study Data Specifications v1.0 to draft eCTD Guidance. This specification references the CDISC SDTM for data tabulation datasets

Electronic Common Technical Document (eCTD)

- Draft Guidance for Industry on Providing Regulatory Submissions in Electronic Format--Human Pharmaceutical Applications and Related Submissions. (Posted 8/28/2003)
 - *Federal Register Notice* [\[TXT\]](#) [\[PDF\]](#)
 - [The Draft Guidance](#) 

Specifications

- [eCTD Backbone Files Specification for Module 1](#) 
- [eCTD Backbone File Specification for Modules 2 through 5](#) 
- [eCTD Backbone File Specification for Study Tagging Files](#) 
- [FDA eCTD Table of Contents Headings and Hierarchy](#) 
- [Study Data Specifications](#)  **New!!** (Posted 7/21/2004)

Define-XML HISTORY AND BACKGROUND

- **March 2005** - Study Data Specifications v1.1 Update: Specifications for Data Set Documentation includes:
 - Data definitions
 - Annotated Case Report Forms (CRFs)

*“The specification for the data definitions for datasets provided using the **CDISC SDTM** is included in the Case Report Tabulation Data Definition Specification (**define.xml**) developed by the CDISC define.xml Team”*

- For datasets not prepared using the CDISC SDTM specifications, consult Appendix 2 for information concerning the preparation of a define.pdf data definition file.

Define-XML HISTORY AND BACKGROUND

- **June 2011** – Study Data Specifications v1.6:
The specification for the data definitions for datasets provided using the *CDISC SDTM IG* or *SEND IG* is included in the Case Report Tabulation Data Definition Specification ...”
- **July 2012** – Study Data Specifications v2.0:
The specification for the data definitions for datasets provided using *CDISC* is included in the Case Report Tabulation Data Definition Specification ...”

Define-XML HISTORY AND BACKGROUND

- **December 2011** CDER Common Data Standards Issues Document (Version 1.1):

“A critical component of data submission is the define file. A **properly functioning** define.xml file is an important part of the submission of standardized electronic datasets and **should not be considered optional.**”

“Additionally, sponsors should make certain that every data variable’s code list, origin, and derivation is **clearly and easily accessible** from the define file. An insufficiently documented define file is a common deficiency that reviewers have noted.”



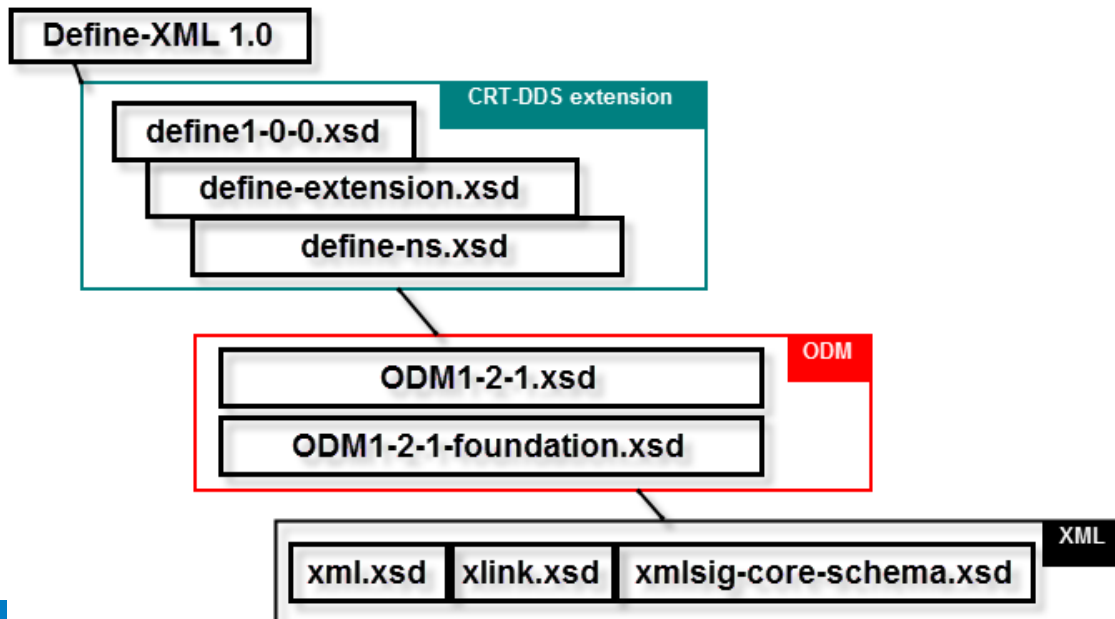
Don't give this message with a define.xml file

WHAT IS DEFINE-XML ?



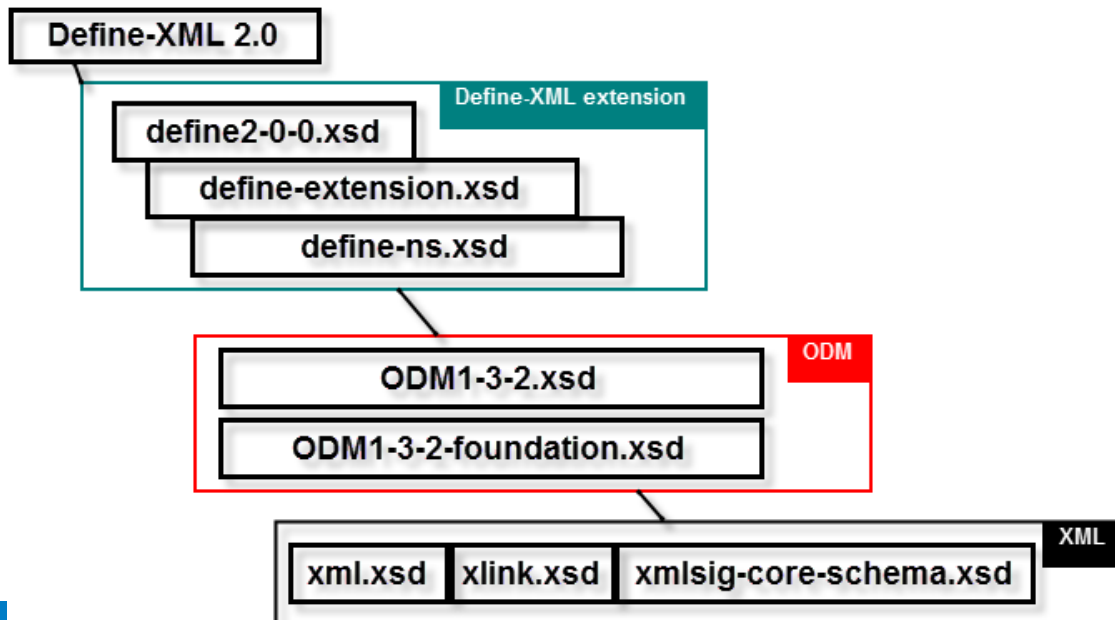
Define-XML WHAT IS IT ?

- Extension of the CDISC Operational Data Model (**ODM**), a vendor neutral, platform independent XML format to facilitate the archival and interchange of the metadata and data for clinical research
- Define-XML: **metadata** structures to describe data sets
- Maintained by CDISC' s **XML Technologies Team**



Define-XML WHAT IS IT ?

- Extension of the CDISC Operational Data Model (**ODM**), a vendor neutral, platform independent XML format to facilitate the archival and interchange of the metadata and data for clinical research
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Define-XML WHAT IS IT ?

- Case Report Tabulation Data Definition Specification, (CRT-DDS), or commonly known as “define.xml”, is not just for SDTM, SEND or ADaM but can even be used for non-submission, proprietary data sets.
- In version 2 the standard is called "**Define-XML**"
- **define.xml** is the file, an instance of the Define-XML standard.

Define-XML SPECIFICATIONS



CDISC Define-XML Specification Version 2.0

Prepared by

CDISC Define-XML Team

Notes to Readers

- This is the specification for Version 2.0 of the CDISC Define-XML standard.
- This is an update of the Case Report Tabulation Data Definition Version 1.0.0 Specification.

Revision History

Date	Version	Summary of Changes
2005-02-05	1.0.0	This is the official implementation version of the Case Report Tabulation Data Definition specification.
2005-02-09	1.0.0	Administrative update.
2009-11-27	2.0.0.1	Draft specification for Define-XML 2.0.0
2011-09-16	2.0.0.2	Updated Define-XML 2.0.0 specification in new format
2012-07-23	2.0.0.3	Update for SRC review and draft publication.
2012-08-31	2.0DRAFT	Public review DRAFT of version 2.0 of the Define-XML Standard.
2013-03-05	2.0.0	Production version of the Define-XML v2.0 Specification



Strength Through Collaboration

Clinical Data Interchange Standards Consortium

Specification for the Operational Data Model (ODM)

Version 1.3.2 Production
Source File: ODM1-3-2.htm
Last Update: 2013-02-05

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An official copy of this document is available on the ODM page of the CDISC website <http://www.cdisc.org/odm>.

Please see [Section 7.0](#) for Review Period; Licensing Obligations, Representations and Warranties; Limitations of Liability, and Disclaimers.

This document is the specification for ODM version 1.3.2. A list of additions and changes since ODM version 1.3.0 is provided in [Section 2.5 Changes from Previous Versions](#). All changes are backward compatible -- ODM XML files conforming to the ODM version 1.2, 1.2.1, 1.3.0 or 1.3.1 schema will also conform to the ODM version 1.3.2 schema.

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Define-XML WHAT IS IT ?

- Provides **metadata** about:
 - **Study**
 - Name, Description, Protocol name
 - **Domains**
 - Name, Label, Structure, Class, Purpose, Keys, Dataset Location, ...
 - **Variables**
 - Name, Label, Data Type, Length, Display Format, Controlled Terms, Origin, Derivations, Comments...
 - **Controlled Terminology / Dictionaries**
 - **Derivations** (algorithms, computations, methods)
 - Supporting **Documents** (aCRF, Supplemental Data Definitions, ..)
 - (Parameter) **Value Level Metadata**
 - Concepts as **SuppQuals**, **Split domains** ...

Define-XML WHAT IS IT ?

- Specification for describing data sets (metadata)



- Does **not** describe how this metadata should be displayed
- Display** is not part of the standard

Dataset	Description	Structure	Purpose	Keys	Location
AE	Adverse Events	Events - One record per adverse event per subject	Tabulation	STUDYID USUBJID AEDCOD AESTDTC	Adverse Events SAS transport file
CE	Clinical Events	Events - One record per event per subject	Tabulation	STUDYID USUBJID CETERM CESTDTC	Clinical Events SAS transport file
CM	Concomitant Medications	Interventions - One record per recorded medication occurrence or constant-dosing interval per subject	Tabulation	STUDYID USUBJID CMTR1 CMSTDTC	Concomitant Medications SAS transport file
CO	Comments	Special Purpose Domains - One record per comment per subject	Tabulation	STUDYID USUBJID COSEQ	Comments SAS transport file
DA	Drug Accountability	Findings - One record per drug accountability finding per subject	Tabulation	STUDYID USUBJID DATESTCD DADTC	Drug Accountability SAS transport file
DM	Demographics	Special Purpose Domains - One record per subject	Tabulation	STUDYID USUBJID	Demographics SAS transport file
DS	Disposition	Events - One record per disposition status or protocol milestone per subject	Tabulation	STUDYID USUBJID DSDECOD DSSTDTC	Disposition SAS transport file

- Annotated Case Report Form - Reviewers Guide - Datasets - Value Level Metadata - Computational Algorithms - Controlled Terms

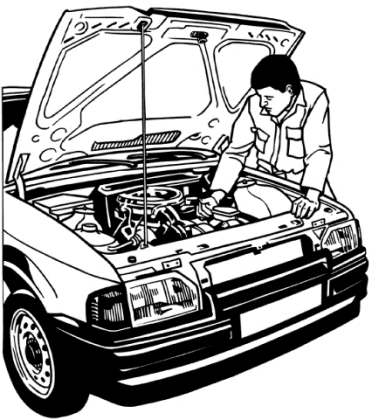
Dataset	Description	Class	Structure	Purpose	Keys
TA	Trial Arms	Trial Design	One record per planned Element per Arm	Tabulation	STUDYID, ARMCD, TAETORD
TE	Trial Elements	Trial Design	One record per planned Element	Tabulation	STUDYID, ETCD
TI	Trial Inclusion/Exclusion Criteria	Trial Design	One record per I/E criterion	Tabulation	STUDYID, IETESTCD
TS	Trial Summary	Trial Design	One record per trial summary parameter value	Tabulation	STUDYID, TSPARMCD, TSSEQ
TV	Trial Visits	Trial Design	One record per planned Visit per Arm	Tabulation	STUDYID, VISITNUM, ARMCD
DM	Demographics	Special Purpose	One record per subject	Tabulation	STUDYID, USUBJID

- Annotated Case Report Form - SDTM Datasets - Value Level Metadata - Controlled Terms - External Dictionary - Computational Algorithms
--

SDTM Datasets for Study CDISCPILOT01

Dataset	Description	Class	Structure	Purpose
TA	Trial Arms	Trial Design	One record per planned Element per Arm	Tabulation
TE	Trial Elements	Trial Design	One record per planned Element	Tabulation
TI	Trial Inclusion/Exclusion Criteria	Trial Design	One record per I/E criterion	Tabulation
TS	Trial Summary	Trial Design	One record per trial summary parameter value	Tabulation
TV	Trial Visits	Trial Design	One record per planned Visit per Arm	Tabulation
DM	Demographics	Special Purpose	One record per subject	Tabulation
SE	Subject Elements	Special Purpose	One record per actual Element per subject	Tabulation
SV	Subject Visits	Special Purpose	One record per actual visit per subject	Tabulation
CM	Concomitant Medications	Interventions	One record per recorded medication occurrence or constant-dosing interval per subject	Tabulation
EX	Exposure	Interventions	One record per constant dosing	Tabulation

Define-XML WHAT IS IT ?



```
<ItemGroupDef OID="ADSL" Name="ADSL" Repeating="No" IsReferenceData="No"
  Purpose="Analysis" def:Label="Subject-Level Analysis"
  def:Structure="one record per subject" def:DomainKeys="USUBJID"
  def:Class="ADSL" def:ArchiveLocationID="Location.ADSL">
  <ItemRef ItemOID="ADSL.STUDYID" OrderNumber="1" Mandatory="No"/>
  <ItemRef ItemOID="ADSL.USUBJID" OrderNumber="2" Mandatory="No"/>
  <ItemRef ItemOID="ADSL.SUBJID" OrderNumber="3" Mandatory="No"/>
  ...
  <ItemRef ItemOID="ADSL.ARM" OrderNumber="6" Mandatory="No"/>
  ...

  <def:leaf ID="Location.ADSL" xlink:href="adsl.xpt">
    <def:title>adsl.xpt </def:title>
  </def:leaf>
</ItemGroupDef>
...

<ItemDef OID="ADSL.ARM" Name="ARM" DataType="text" Length="20"
  Origin="Derived" Comment="DM.ARM" def:Label="Description of Planned Arm">
  <CodeListRef CodeListOID="ARM"/>
</ItemDef>
```

ISSUES WITH DEFINE-XML 1.0



Define-XML 1.0 ISSUES – VALUE LEVEL METADATA

- (Parameter) Value Level Metadata defines **metadata** for a **variable** under a specific **condition**
- Needed in the highly normalized data structure of SDTM, SEND and ADaM (generally one record per subject per test code or parameter per visit or observation)
- Examples:
 - **VSORRES**, **VSSTRESN** or **VSTRESU** based on the value of **VSTESTCD**
 - SuppQuals: **QVAL** bases on the value of **QNAM**
 - **LBORRES** based on the value of **LBCAT**, **LBSPEC**, **LBMETHOD**, **LBTESTCD**
 - **AVAL**, **BASE**, **CHG** based on the value of **PARAMCD**

Define-XML 1.0 ISSUES – VALUE LEVEL METADATA

```
<ItemDef OID="I.VSTESTCD"
  Name="VSTESTCD" DataType="text"
  Length="8" Origin="CRF Page 9"
  def:Label="Vital Signs Test Short Name">
  <def:ValueListRef ValueListOID="VL.VSTESTCD" />
</ItemDef>
```

USUBJID	VSTESTCD	VSTEST	VSORRES	VSSTRESN	VSSTRESC
00001	HEIGHT	Height	183	183	183
00001	WEIGHT	Weight	88.5	88.5	88.5
00001	FRMSIZE	Body Frame Size	Large		Large

Value Level Metadata						
Source Dataset	Source Variable	Value	Label	Type	Controlled Terms or Format	Origin
VS	VSTESTCD	HEIGHT	Height	integer	3.0	CRF Page 5
VS	VSTESTCD	WEIGHT	Weight	float	5.1	CRF Page 5
VS	VSTESTCD	FRMSIZE	Body Frame Size	text	SMALL, MEDIUM, LARGE	CRF Page 6

Define-XML 1.0 ISSUES – VALUE LEVEL METADATA

```
<ItemDef OID="IT.VS.VSTESTCD"
  Name="VSTESTCD" DataType="text"
  Length="8" Origin="CRF Page 9"
  def:Label="Vital Signs Test Short Name">
  <def:ValueListRef ValueListOID="VL.VSTESTCD"/>
</ItemDef>

<def:ValueListDef OID="VL.VSTESTCD">
  <ItemRef ItemOID="IT.VS.VSTESTCD.HEIGHT" OrderNumber="1" Mandatory="No"/>
  <ItemRef ItemOID="IT.VS.VSTESTCD.WEIGHT" OrderNumber="2" Mandatory="No"/>
  <ItemRef ItemOID="IT.VS.VSTESTCD.FRMSIZE" OrderNumber="3" Mandatory="No"/>
  ...
</def:ValueListDef>

<ItemDef OID="IT.VS.VSTESTCD.FRMSIZE"
  Name="FRMSIZE" DataType="text" Length="6"
  Origin="CRF Page 11" def:Label="Body Frame Size">
  <CodeListRef CodeListOID="CL.SIZE"/>
</ItemDef>

<ItemDef OID=" IT.VS.VSTESTCD.HEIGHT"
  Name="HEIGHT" DataType="float" SignificantDigits="1"
  Length="5" Origin="CRF Page 11" def:Label="Height"/>

<ItemDef OID=" IT.VS.VSTESTCD.WEIGHT"
  Name="WEIGHT" DataType="float" SignificantDigits="1"
  Length="4" Origin="CRF Page 11" def:Label="Weight"/>
```

Define-XML 1.0 ISSUES – VALUE LEVEL METADATA

Which variable are we actually describing?
VSORRES, VSSTRESN, VSSTRESC ???

```
<ItemDef OID="IT.VS.VSTESTCD.FRMSIZE"
  Name="FRMSIZE" DataType="text" Length="6"
  Origin="CRF Page 11" def:Label="Body Frame Size">
  <CodeListRef CodeListOID="CL.SIZE"/>
</ItemDef>

<ItemDef OID=" IT.VS.VSTESTCD.HEIGHT"
  Name="HEIGHT" DataType="float" SignificantDigits="1"
  Length="5" Origin="CRF Page 11" def:Label="Height"/>

<ItemDef OID=" IT.VS.VSTESTCD.WEIGHT"
  Name="WEIGHT" DataType="float" SignificantDigits="1"
  Length="4" Origin="CRF Page 11" def:Label="Weight"/>
```

USUBJID	VSTESTCD	VSTEST	VSORRES	VSSTRESN	VSSTRESC
00001	HEIGHT	Height in cm	183	183	
00001	WEIGHT	Weight in kg	88.5	88.5	
00001	FRAME	Body Frame Size	Large		Large

Define-XML 1.0 ISSUES – VALUE LEVEL METADATA

Analysis Dataset Lab Hy's Law (ADLBHY) [adlbhy.xpt](#)

Variable	Label	Type	Length	Display Format	Code List / Controlled Terms	Source/Derivation
STUDYID	Study Identifier	text	12			ADSL.STUDYID
SUBJID	Subject Identifier for the Study	text	4			ADSL.SUBJID
USUBJID	Unique Subject Identifier	text	11			ADSL.USUBJID
AVAL	Analysis Value	float	8			
BASE	Baseline Value	float	8			
A1LO	Analysis Range 1 Lower Limit	float	8			

Parameter Value List - ADLBHY [AVAL]

Source Variable	Where PARAMCD=	Where PARAM=	Type	Length	Display Format	Code List / Controlled Term	Source/Derivation/Comments
AVAL	ALT	Alanine Aminotransferase (U/L)	integer	8			ADLBC.AVAL
AVAL	AST	Aspartate Aminotransferase (U/L)	integer	8			ADLBC.AVAL
AVAL	BILI	Bilirubin (umol/L)	float	8	6.2		ADLBC.AVAL
AVAL	BILIHY	Bilirubin 1.5 x ULN	integer	8		YNN	for a given visit, if param='BILI' and param='BILI' then aval=0

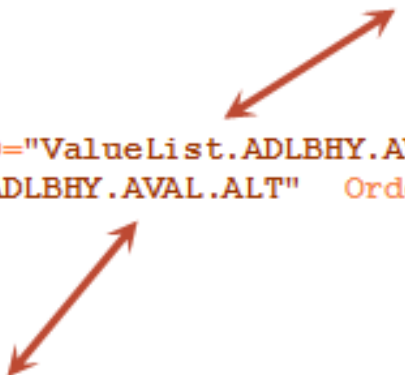
Define-XML 1.0 ISSUES – VALUE LEVEL METADATA

```
<ItemDef OID="ADLBHY.PARAMCD" Name="PARAMCD" DataType="text"
  Length="8" Origin="Derived" def:Label="Parameter Code" >

<ItemDef OID="ADLBHY.AVAL" Name="AVAL" DataType="float"
  Length="8" SignificantDigits="2" Origin="Derived" def:Label="Analysis Value" >
  <def:ValueListRef ValueListOID="ValueList.ADLBHY.AVAL"/>
</ItemDef>

<def:ValueListDef OID="ValueList.ADLBHY.AVAL">
  <ItemRef ItemOID="ADLBHY.AVAL.ALT" OrderNumber="13" Mandatory="No"/>
  ...
</def:ValueListDef>

<ItemDef OID="ADLBHY.AVAL.ALT" Name="ALT" DataType="integer" Length="8"
  Origin="Derived" Comment="ADLBC.AVAL" def:Label="Alanine Aminotransferase (U/L)" />
```



“Where PARAMCD=“ and “Where
PARAM=“ were hardcoded in the
stylesheet.

Define-XML 1.0 ISSUES – VALUE LEVEL METADATA

- Define-XML 1.0 does not fully support the use cases in SDTM and ADaM in a fully machine readable way:
 - Variable Level Metadata for more than one variable in a domain
 - Variable Level Metadata based on a more complicated condition than equal to one variable value
- This can lead to operability problems

Define-XML 1.0 ISSUES – CODE LISTS

- In Define-XML 1.0 Code Lists always need **Codes** and **Decodes**
- SDTM and ADaM only need a list of allowed values in most cases
- The solution in 1.0 is to have identical **Codes** and **Decodes**

```
<CodeList OID="ACN" Name="ACN" DataType="text">
  <CodeListItem CodedValue="DOSE NOT CHANGED">
    <Decode>
      <TranslatedText>DOSE NOT CHANGED</TranslatedText>
    </Decode>
  </CodeListItem>
```

Define-XML 1.0 ISSUES – CODE LISTS

- In Define-XML 1.0 there is no link with the CDISC / NCI Controlled Terminology

CDISC Controlled Terminology ADaM - 2011-01-07

C81224 - DTYPE - Derivation Type

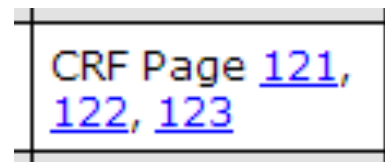
Codelist extensible: Yes

NCI Code	CDISC Submission Value	CDISC Synonym	CDISC Definition	NCI Preferred Term
C81209	AVERAGE		Average: A data derivation technique which calculates a subject's average value over a defined set of records.	Average of Value Derivation Technique
C92225	BC		Best Case: A data imputation technique which populates missing values with the best possible outcome.	Best Case Imputation Technique
C81201	BLOCF		Baseline Observation Carried Forward: A data imputation technique which populates missing values with the subject's nonmissing baseline observation.	Baseline Observation Carried Forward Imputation Technique
C92226	BOCF		Best Observation Carried Forward: A data imputation technique which populates missing values with the subject's best-case nonmissing value.	Best Observation Carried Forward Imputation Technique
C82866	ENDPOINT		Endpoint: A data derivation technique which calculates a subject's analysis end point value.	Endpoint Value Derivation Technique

Define-XML 1.0 ISSUES – EXTERNAL DOCUMENT LINKS

- Define-XML 1.0 has very limited support for linking
- How do we get from:

Origin = “[CRF Pages 121, 122, 123](#)” to real links ?
.... parsing and hardcoding



- How can we link from datasets, variables or methods to supporting documents ?

Comment =

“[See Study Data Reviewers Guide page 14](#)”

- How about linking to Named Destinations or ranges of pages ?

Define-XML 1.0 ISSUES – SPECIFICATION

- The Define-XML 1.0 specification is ambiguous in several aspects:
 - Datatypes – does a date have a “date” or “text” attribute?
 - Do we need a code list reference for ISO8601
- There is no specification for “split domains”, which were introduced after the release of 1.0
- Not many examples in the Define-XML 1.0 specification

WHAT'S NEW IN DEFINE-XML 2.0 ?



Define-XML 2.0 WHAT'S NEW

- Based on ODM 1.3.2
- Define-XML version 2.0 can be used to transmit metadata for the following CDISC standards:
 - SDTM Implementation Guide Versions 3.1.2 and higher
 - ADaM Implementation Guide Versions 1.0 and higher
 - SEND Implementation Guide Versions 3.0 and higher
- **Not backward compatible** to allow for a clearer and less ambiguous model
- Production version since March 2013
(Minor stylesheet update April 2013)

<http://www.cdisc.org/define-xml>

Define-XML 2.0 WHAT'S NEW

- Refinements to all model components to reflect
 - Implementation experience
 - Improved machine readability
 - More explicit metadata
 - SDTM, SEND and ADaM have matured since 2005
- New features
 - Flexible and explicit definition of Value Level metadata include Where Clauses
 - Better support for CDISC Controlled Terminology
 - Enhanced documentation of data origin/source
 - Better handling of comments

Define-XML 2.0 WHAT'S NEW

- Deprecated: replaced by ODM 1.3.2 or enhanced

Element	Component	Replaced by
MetaDataVersion	def:ComputationalMethod	MethodDef element
ItemGroupDef	def:Label	Description element
ItemGroupDef	def:DomainKeys	@KeySequence attribute
ItemDef	def:Label	Description element
ItemDef	def:ComputationMethodOID	@MethodOID attribute
ItemDef	Origin	New def:Origin element
ItemDef	Comment	New def:Comment element
CodeListItem	def:Rank	ODM Rank attribute

Define-XML 2.0 WHAT' S NEW – VALUE LEVEL METADATA

- Can now be provided for any dataset variable
- Condition can be based on values of multiple variables with more complicated conditions (not just EQUAL)
- Examples:
 - VSTESTCD **EQ** "SYSBP" and VSPOS **EQ** "STANDING"
 - PARAMCD **IN** ("ACITM01", "ACITM02", ... , "ACITM14")
 - PARAMCD **NE** "ACTTOT"
- Available: LT, LE, GT, GE, EQ, NE, IN, NOTIN
- Unambiguous interpretation by a computer

Define-XML 2.0 WHAT' S NEW – VALUE LEVEL METADATA

Parameter Value List - ADQSADAS [AVAL]

Variable	Where	Type	Length / Display Format	Controlled Terms or Format	Origin	Derivation/Comment
AVAL	PARAMCD IN ("ACITM01" (Word Recall Task) , "ACITM02" (Naming Objects And Fingers (Refer To 5 C) .	integer	8		Derived	QS.QSSTRESN where QSTESTCD=PARAMCD
	speed) , "ACITM14" (Recall Of Test Instructions))					
AVAL	PARAMCD EQ ACTOT (Adas-Cog(11) Subscore)	integer	8		Derived	Sum of ADAS scores for items 1, 2, 4, 5, 6, 7, 8, 11, 12, 13, and 14, see Analysis Data Reviewers Guide (Page 3) for details on adjusting for missing values. Analysis Data Reviewer's Guide (analysis-data-reviewers-guide.pdf)

Define-XML 2.0 WHAT'S NEW – VALUE LEVEL METADATA

```
<ItemDef OID="IT.ADQSADAS.AVAL" Name="AVAL" SASFieldName="AVAL"
  DataType="integer" Length="8">
  <Description>
    <TranslatedText xml:lang="en">Analysis Value</TranslatedText>
  </Description>
  <def:ValueListRef ValueListOID="VL.ADQSADAS.AVAL" />
</ItemDef>

<def:ValueListDef OID="VL.ADQSADAS.AVAL">
  <ItemRef ItemOID="IT.ADQSADAS.QSSEQ.ACITM01-ACITM14" Mandatory="No">
    <def:WhereClauseRef WhereClauseOID="WC.ADQSADAS.QSSEQ.ACITM01-ACITM14" />
  </ItemRef>
  <ItemRef ItemOID="IT.ADQSADAS.QSSEQ.ACTOT" Mandatory="No">
    <def:WhereClauseRef WhereClauseOID="WC.ADQSADAS.QSSEQ.ACTOT" />
  </ItemRef>
</def:ValueListDef>
```

Define-XML 2.0 | WHAT'S NEW – VALUE LEVEL METADATA

```
<def:WhereClauseDef OID="WC.ADQSADAS.AVAL.ACITM01-ACITM14">
  <RangeCheck Comparator="IN" SoftHard="Soft" def:ItemOID="IT.ADQSADAS.PARAMCD">
    <CheckValue>ACITM01</CheckValue>
    ...
    <CheckValue>ACITM14</CheckValue>
  </RangeCheck>
</def:WhereClauseDef>

<def:WhereClauseDef OID="WC.ADQSADAS.AVAL.ACTOT">
  <RangeCheck Comparator="EQ" SoftHard="Soft" def:ItemOID="IT.ADQSADAS.PARAMCD">
    <CheckValue>ACTOT</CheckValue>
  </RangeCheck>
</def:WhereClauseDef>
```

Define-XML 2.0 WHAT' S NEW – CODE LISTS

- Controlled Terminology can now be defined using **Enumerated Items**
- Also notice the new **OrderNumber** attribute for defining display order

```
<CodeList OID="CL.ACN" Name="Action Taken with Study Treatment" DataType="text">
  <EnumeratedItem CodedValue="DOSE NOT CHANGED" OrderNumber="1" />
  <EnumeratedItem CodedValue="DOSE REDUCED" OrderNumber="2" />
  <EnumeratedItem CodedValue="DRUG INTERRUPTED" OrderNumber="3" />
  <EnumeratedItem CodedValue="DRUG WITHDRAWN" OrderNumber="4" />
</CodeList>
```

Define-XML 2.0 WHAT'S NEW – CODE LISTS

- Linking Code Lists to CDISC / NCI Controlled Terminology

Trial Summary Parameter Test Code [CL.TSPARMCD, C66738]

Permitted Value (Code)	Display Value (Decode)
ADDON [C49703]	Added on to Existing Treatments
AGEMAX [C49694]	Planned Maximum Age of Subjects
AGEMIN [C49693]	Planned Minimum Age of Subjects
AGESPAN [C20587]	Age Span
AGEU [*]	Age Unit
DOSE [C25488]	Dose per Administration

...

TITLE [C49802]	Trial Title
TPHASE [C48281]	Trial Phase Classification
TRT [C41161]	Investigational Therapy or Treatment
TTYPE [C49660]	Trial Type

* Extended Value

Define-XML 2.0 WHAT'S NEW – CODE LISTS

- Linking Code Lists to CDISC / NCI Controlled Terminology

```
<CodeList OID="CL.TSPARMCD" Name="Trial Summary Parameter Test Code"
  DataType="text" SASFormatName="$TSPARMC">
  <CodeListItem CodedValue="ADDON">
    <Decode>
      <TranslatedText xml:lang="en">Added on to Existing Treatments</TranslatedText>
    </Decode>
    <Alias Name="C49703" Context="nci:ExtCodeID"/>
  </CodeListItem>
  <CodeListItem CodedValue="AGEU" def:ExtendedValue="Yes">
    <Decode>
      <TranslatedText xml:lang="en">Age Unit</TranslatedText>
    </Decode>
  </CodeListItem>
  ...

  <CodeListItem CodedValue="TTYE">
    <Decode>
      <TranslatedText xml:lang="en">Trial Type</TranslatedText>
    </Decode>
    <Alias Name="C49660" Context="nci:ExtCodeID"/>
  </CodeListItem>
  <Alias Name="C66738" Context="nci:ExtCodeID"/>
</CodeList>
```

Define-XML 2.0 WHAT' S NEW – LINKING TO DOCUMENTS

- Linking from an SDTM variable to a CRF Page

```
<ItemDef OID="IT.AE.AEACN" Name="AEACN" DataType="text"
  Length="30" SASFieldName="AEACN">
  <Description>
    <TranslatedText xml:lang="en">Action Taken with Study Treatment</TranslatedText>
  </Description>
  <CodeListRef CodeListOID="CL.ACN"/>
  <def:Origin Type="CRF">
    <def:DocumentRef leafID="LF.blankcrf">
      <def:PDFPageRef PageRefs="21" Type="PhysicalRef"/>
    </def:DocumentRef>
  </def:Origin>
</ItemDef>

<def:leaf ID="LF.blankcrf" xlink:href="blankcrf.pdf">
  <def:title>Annotated Case Report Form</def:title>
</def:leaf>
```

Define-XML 2.0 WHAT'S NEW – LINKING TO DOCUMENTS

- Linking from a derivation to an external document

```
<def:ValueListDef OID="VL.ADQSADAS.AVAL">  
  <ItemRef ItemOID="IT.ADQSADAS.AVAL.ACTOT" Mandatory="No"  
    MethodOID="MT.ADQSADAS.AVAL.ACTOT">  
    <def:WhereClauseRef WhereClauseOID="WC.ADQSADAS.AVAL.ACTOT" />  
  </ItemRef>
```

```
<MethodDef OID="MT.ADQSADAS.AVAL.ACTOT"  
  Name="CM.ADQSADAS.AVAL.ACTOT" Type="Computation">  
  <Description>  
    <TranslatedText xml:lang="en">Sum of ADAS scores for items 1, 2, 4,  
      5, 6, 7, 8, 11, 12, 13, and 14, see Analysis Data Reviewers Guide  
      (Page 3) for details on adjusting for missing values.</TranslatedText>  
  </Description>  
  <def:DocumentRef leafID="LF.ADRG">  
    <def:PDFPageRef PageRefs="3" Type="PhysicalRef" />  
  </def:DocumentRef>  
</MethodDef>
```

Define-XML 2.0 WHAT'S NEW – LINKING TO DOCUMENTS

- Linking from a dataset or variable to an external document

```
<ItemGroupDef OID="IG.ADSL" Name="ADSL" SASDatasetName="ADSL"
...
  <def:CommentOID="COM.ADSL" def:ArchiveLocationID="LF.ADSL">
    <Description>
      <TranslatedText xml:lang="en">Subject-Level Analysis</TranslatedText>
    </Description>
  ...
</def:CommentDef OID="COM.ADSL">
  <Description>
    <TranslatedText>Screen Failures are excluded since they are not needed for
      this study analysis. See Reviewers Guide, section 2.1 for more
      details.</TranslatedText>
  </Description>
  <def:DocumentRef leafID="LF.ReviewersGuide">
    <def:PDFPageRef PageRefs="section2.1" Type="NamedDestination"/>
  </def:DocumentRef>
</def:CommentDef>

<def:leaf ID="LF.ReviewersGuide" xlink:href="reviewersguide.pdf">
  <def:title>Reviewers Guide</def:title>
</def:leaf>
```

Define-XML 2.0 WHAT'S NEW – LINKING TO VARIABLES

- Linking from an ADaM variable to a Predecessor (traceability)

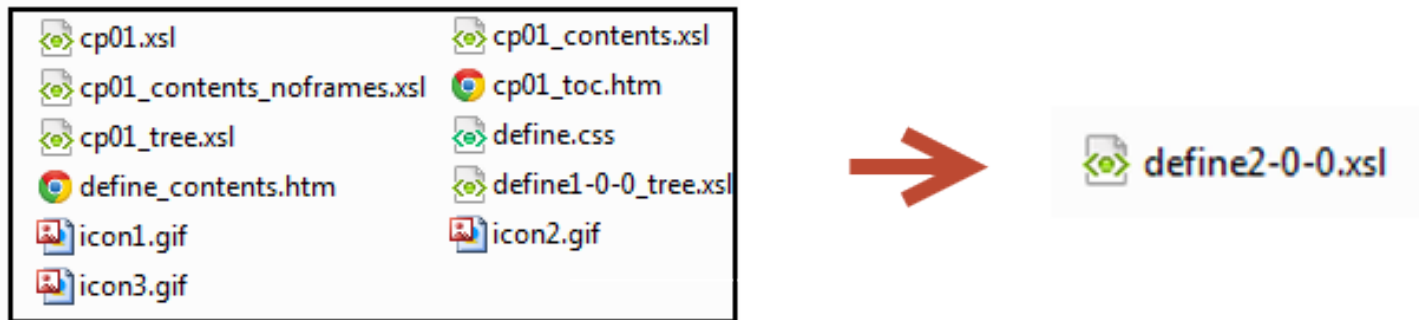
```
<ItemDef OID="IT.ADQSADAS.T RTP" Name="RTP"
  SASFieldName="RTP" DataType="text" Length="20">
  <Description>
    <TranslatedText xml:lang="en">Planned Treatment</TranslatedText>
  </Description>
  <CodeListRef CodeListOID="CL.ARM" />
  <def:Origin Type="Predecessor">
    <Description>
      <TranslatedText xml:lang="en">ADSL.TRT01P</TranslatedText>
    </Description>
  </def:Origin>
</ItemDef>
```

DISPLAYING DEFINE-XML



Define-XML DISPLAY

- The Define-XML standard does not dictate how a **stylesheet** should display a **define.xml** file.
- An example stylesheet is provided, however this can be altered to satisfy alternate visualization needs.
- The example stylesheet is only one file



Define-XML DISPLAY

- The example stylesheet conforms to web standards and follows accessibility guidelines
- It should behave much better than older stylesheets
- Uses JavaScript, but degrades gracefully when JavaScript is disabled
- Printing looks quite acceptable
- It might make sense to also submit the HTML rendition; since not every browser allows rendition of the stylesheet

NEXT STEPS



Define-XML NEXT STEPS

- Validation Requirements for FDA submissions
 - Define unambiguous business rules, that tools can implement
- Implementation Guide
 - No massive document, but incremental
- Analysis Results Metadata extension
 - Under development
- Pilot – Define-XML v2 is already accepted!!



For Industry

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Data Standards

Study Data Standards

[Study Data Standards for Regulatory Submissions](#)

[Janus Clinical Trials Repository \(CTR\) Project](#)

[Standard for Exchange of Non-Clinical Data](#)

[Study Design Standard](#)

[Study Participation Standard](#)

[Subject Data Standard](#)

Study Data Standards Resources

[Sign up for email updates.](#)

[CBER/CDER Study Data Standards for Regulatory Submissions Position Statement](#)

1. Study Data Standards in Current Use

Please refer to the following standards and resources for study data submissions to FDA.

For Center-specific resources, please [click here](#).

1.1 Study Data Specifications

- Specifications for submitting animal and human study datasets in electronic format: [Study Data Specifications](#) (PDF).

1.2 Study Data File Format Standards

- [SAS Transport Version 5](#)
 - Organization – CBER, CDER, CDRH
 - Use for Study datasets
- [XML Version 1.0](#)
 - Organization – CBER, CDER
 - Use for SDTM and ADaM define.xml file
- [PDF Versions 1.4/1.5/1.6](#)
 - Organization – CBER, CDER, CDRH
 - Use for SDTM and ADaM define.pdf
- [American Standard Code for Information Interchange \(ASCII\)](#)
 - Organization – CBER, CDER, CDRH
 - Use for analysis program files

1.3 Study Data Exchange and Analysis Standards

- [CDISC define.xml Version 2.0](#)
 - Organization – CBER, CDER, CDRH
 - Use for study data definition specification
- [CDISC define.xml Version 1.0](#)
 - Organization – CBER, CDER, CDRH
 - Use for study data definition specification





Thank You !

Questions ?



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