PP13

It's Time to Move, Time to Move to Define-XML 2.1

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Abstract

As of March 2023, specifically for any study started on or after March 15, 2023, **FDA recommends the use of Define-XML 2.1**.

This new version, contains some good improvements for both **human and machine "readability."** Most off-the-shelf software already have integrated support for it, including the necessary metadata. For internally developed software relying on ad-hoc metadata repositories and tools like SAS macros, **adopting Define-XML 2.1 requires additional metadata** and the **deprecation of certain elements** from the previous version.

For those planning to move to Define-XML 2.1 for a study that has already been started and making use of Define-XML 2.0, **migration from 2.0 to 2.1 is straightforward**.

With this poster we would like to introduce key define 2.1 enhancements and Cytel experience transitioning to the new version.

Origin/Source

- The Origin element now has an accompanying attribute: Source.
- CRF and eDT values of **Origin:Type** from v2.0 are now deprecated:
  - CRF in v2.1 → Origin:Type=Collected
    Origin:Source=Investigator
  - eDT in v2.1 → Origin:Type=Collected
    Origin:Source=Vendor
- The Source attribute may have the following values:
  - Subject
  - Investigator
  - Vendor
  - Sponsor
  - <blank> (only when Origin:Type=Predecessor)

Origin/Source (cont.)

define 2.0	define 2.1		Comment
TYPE	TYPE	SOURCE	
CRF	Collected	Investigator	Collected directly in the CRF
eDT	Collected	Subject	Collected by the subject through an instrument
eDT	Collected	Vendor	Received from a central lab e.g., labs, ECG
Derived	Derived	Vendor	Calculated within an EDC e.g., BMI calculated or by an instrument e.g., questionnaire section scores within an ePRO
Derived	Derived	Sponsor	Calculated in SDTM e.g., EPOCH
Assigned	Assigned	Vendor	Coding terms such as MedDRA for AE, or assigned through a third-party adjudication process e.g., best tumor response in an oncology trial
Assigned	Assigned	Sponsor	Assigned in SDTM e.g., --TESTCD, DOMAIN
Protocol	Protocol	Sponsor	Not directly collected but it could be assigned by protocol e.g., VSPOS (Vital Signs Position)
Change to "Origin" element			

Empty Items

- Both the Datasets and Variables elements now have a new attribute **HasNoData=Yes** to indicate empty items, e.g., a domain is included in the package with no records, or a dataset contains a variable where all values are missing.
- Here an example how the stylesheet renders the attribute.

Datasets

Dataset	Description	Class	Structure	Purpose	Keys
SUPPVS [SDTMIG 3.1.2] [No Data]	Supplemental Qualifiers for VS (Vital Signs)	RELATIONSHIP	One record per IDVAR, IDVARVAL, and QNAM value per subject	Tabulation	STUDYID, RDOMAIN, USUBJID, IDVAR, IDVARVAL, QNAM

XS (S Findings) - [Non Standard]

Location: xs.xpt

Variable	Label / Description	Type	Length or Display Format	Controlled Terms or ISO Format	Origin / Source / Method / Comment
XSORRESU [No Data]	Original Units	text	20	Units for S Findings Results	Collected (Source: Vendor) Planned Numeric tests were not performed.

Class/Subclass

The ADaM Datasets now have a new attribute **Subclass** to further classify datasets.

Class	Subclass
BASIC DATA STRUCTURE	NON-COMPARTMENTAL ANALYSIS
BASIC DATA STRUCTURE	POPULATION PHARMACOKINETIC ANALYSIS
BASIC DATA STRUCTURE	TIME-TO-EVENT
MEDICAL DEVICE BASIC DATA STRUCTURE	MEDICAL DEVICE TIME-TO-EVENT
OCCURRENCE DATA BASIC DATA STRUCTURE	ADVERSE EVENT

Multiple Standards

- Previously in v2.0 Standard versions were specified for the entire package. With v2.1 we are now able to specify the **different standards applied in the datasets package**

SDTM Standards	ADaM Standards
SDTMIG 3.1.2	ADaMIG 1.1
SDTMIG 3.2	ADaMIG 1.2
SDTMIG 3.3	
SDTMIG 3.4	
SDTMIG-MD 1.0	

- The Descriptions of different standards can also be documented with the standard.

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

Multiple CT Versions

- Previously in v2.0 Controlled Terminology (CT) version was specified for the entire package. With v2.1 we are now able to specify **different CT versions on the Codelist attribute**.

Study Planned Countries [CDISC/NCI SDTM 2011-12-09]
This is a subset of the ISO-3166 (Country Codes) codelist

Permitted Value (Code)	Display Value (Decode)
USA	United States of America (the)
CAN	Canada
MEX	Mexico

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

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

Comments on Codelist

- With v2.1 we are now able to add **Descriptions or Explanatory text to a Codelist**.
- The following example highlights in yellow a codelist comment

Study Planned Countries [CDISC/NCI SDTM 2011-12-09]
This is a subset of the ISO-3166 (Country Codes) codelist

Permitted Value (Code)	Display Value (Decode)
USA	United States of America (the)
CAN	Canada
MEX	Mexico

References

1) https://www.cdisc.org/standards/data-exchange/define-xml/define-xml-v2-1
2) https://www.lexjansen.com/pharmasug/2022/DS/PharmaSUG-2022-DS-064.pdf
3) https://www.cytel.com/blog/its-time-to-move-time-to-move-to-define-xml-2.1

Has your company already adopting define.xml 2.1?

What was your experience transitioning from version 2.0 to 2.1?

Learn more about define.xml 2.1

Cytel's Experience in Implementing v2.1

- **Transition to version 2.1 was smooth** with studies handled in Pinnacle21 Enterprise
- Some sponsors requested to migrate existing studies to 2.1 from 2.0 → **Created SAS macro for migrating from 2.0 to 2.1** for studies not using Pinnacle21 Enterprise
- Modified **Cytel Standard SDTM and ADaM specs**
- Additional Cytel internal tools were updated
- **Programming Team trained** on define 2.1 changes and enhancements

Cytel

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18-20 September
Silver Spring, MD
CSS 2023
The Computational Science Symposium

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