



PRAHEALTHSCIENCES

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# Barcelona 2016

**Fast Track to Approval:  
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**PRAHEALTHSCIENCES**

Paper CD15 – PhUSE 2016

**How to handle different versions of SDTM & DEFINE generation in a  
Single Study?**

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- Paper Abstract
- SDTM/Define-XML Releases Background – Overview
- Changes from One SDS to Another SDS Version
- Problem Statement & Solutions
- Conclusion

## Paper Abstract

How to handle different versions of SDTM & DEFINE generation in a Single Study?



Submission Data Standards has been evolving over a period of time and it is still subject to revisions by way inclusion of new therapeutic areas in the form of domains and variables under different classifications. As well, the define.xml which provides a quick access to reviewers to go over the submissions once it is imported into JANUS data warehouse. These revisions and amendments does have impact on ongoing and new studies especially studies which are of longer duration in the case of Oncology studies. Longer duration studies would have started with an SDTM v3.1.3 with Define-XML v1.0 file generation for DSMB analysis and other related submissions. During the course of the study, due to revisions, the same study has to be done under a new version say SDTM v3.2 with Define-XML v2.0 generation. This session would be covering the processes and different steps with demo that needs to be taken care while implementing different versions of SDTM standards and Define-XML generation for a single ongoing study

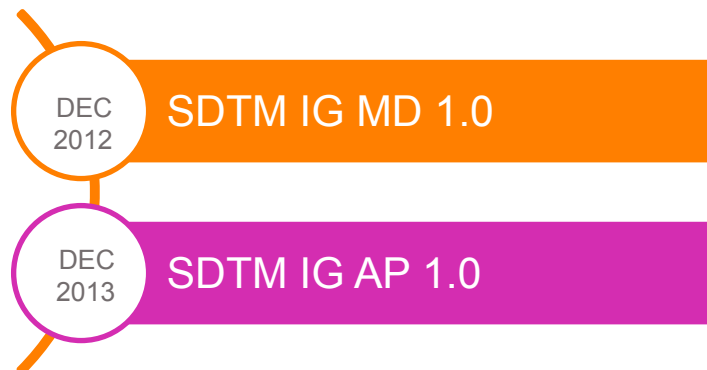
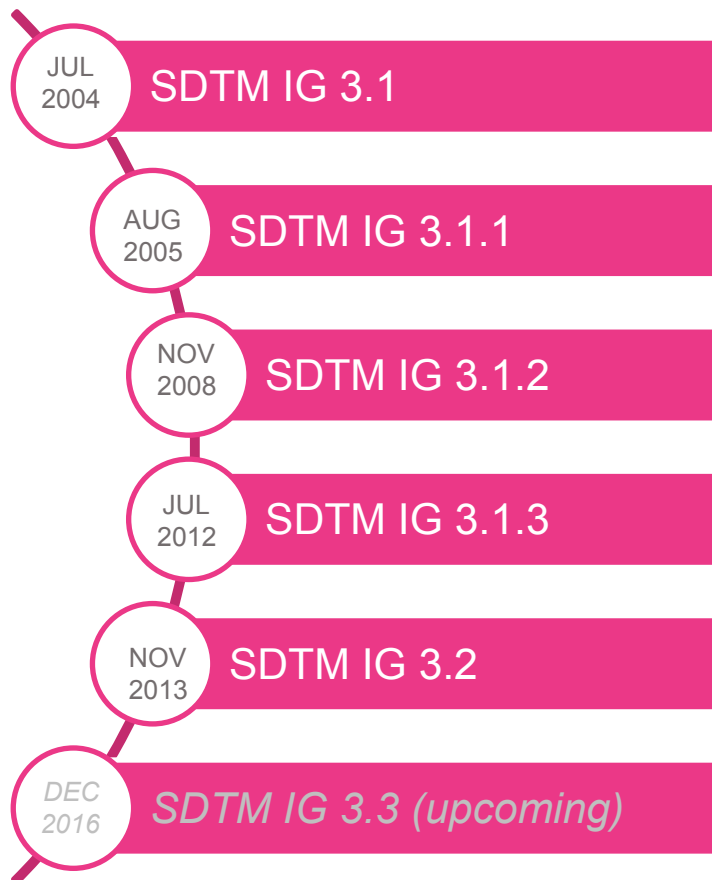


# SDTM/Define-XML Releases

## Background – Overview

# SDTM/Define-XML Releases Background – Overview

## SDTM IG Versions



SDTM first evolved from the Submission Data Model (SDM) as developed by CDISC Submission Data Standards (SDS) Team around 10 years ago. The SDS Team developed a set of consistent data standards for submitting tabulation data for human clinical trials. The SDS team is also responsible for maintaining the compatibility, consistency and conformity of SDTM data standards and associated SDTM Implementation Guide (SDTMIG) as part of the long running Clinical Data Interchange Standards Consortium (CDISC) strategy for harmonizing the submission of clinical trials data.

# SDTM/Define-XML Releases Background – Overview

## Define-XML Versions



### SDTM-IG 3.2

- + Annotated Case Report
- + Reviewers Guide
- + Complex Algorithms
- + Tabulation Datasets
  - Trial Arms (TA)
  - Trial Elements (TE)
  - Trial Inclusion/Exclusion
  - Trial Summary (TS)
  - Trial Visits (TV)
  - Comments (CO)
  - Demographics (DM)
  - Subject Elements (SE)
  - Subject Visits (SV)
  - Concomitant Medication
  - Exposure (EX)
  - Adverse Events (AE)
  - Disposition (DS)
  - Medical History (MH)
  - ECG Test Results (EG)
  - Laboratory Tests Results
  - Laboratory Tests Results
  - Custom Domain (NS)
  - Questionnaires (QS)
  - Vital Signs (VS)
  - Findings About Events
  - Related Records (REL)
  - Supplemental Qualifiers

Date of document generation: 2016-03-16T06:55:43

Stylesheet version: 2013-04-24

### Tabulation Datasets for Study PHUSE2016-Define-XMLV2 (SDTM-IG 3.2)

| Dataset | Description                                        | Class           | Structure                                    | Purpose    | Keys                                       | Location               | Documentation                                                                  |
|---------|----------------------------------------------------|-----------------|----------------------------------------------|------------|--------------------------------------------|------------------------|--------------------------------------------------------------------------------|
| TA      | <a href="#">Trial Arms</a>                         | TRIAL DESIGN    | One record per planned Element per Arm       | Tabulation | STUDYID, ARMCD, TAETORD                    | <a href="#">ta.xpt</a> |                                                                                |
| TE      | <a href="#">Trial Elements</a>                     | TRIAL DESIGN    | One record per planned Element               | Tabulation | STUDYID, ETCD                              | <a href="#">te.xpt</a> |                                                                                |
| TI      | <a href="#">Trial Inclusion/Exclusion Criteria</a> | TRIAL DESIGN    | One record per I/E criterion                 | Tabulation | STUDYID, IETESTCD                          | <a href="#">ti.xpt</a> |                                                                                |
| TS      | <a href="#">Trial Summary</a>                      | TRIAL DESIGN    | One record per trial summary parameter value | Tabulation | STUDYID, TSPARMCD, TSSEQ                   | <a href="#">ts.xpt</a> |                                                                                |
| TV      | <a href="#">Trial Visits</a>                       | TRIAL DESIGN    | One record per planned Visit per Arm         | Tabulation | STUDYID, VISITNUM, ARMCD                   | <a href="#">tv.xpt</a> |                                                                                |
| CO      | <a href="#">Comments</a>                           | SPECIAL PURPOSE | One record per comment per subject           | Tabulation | STUDYID, USUBJID, RDOMAIN, IDVAR, IDVARVAL | <a href="#">co.xpt</a> |                                                                                |
| DM      | <a href="#">Demographics</a>                       | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, USUBJID                           | <a href="#">dm.xpt</a> | See Reviewer's Guide, Section 2.1 Demographics <a href="#">Reviewers Guide</a> |

FEB  
2005

Define-XML 1.0

DEC  
2012

Define-XML 2.0

DEC  
2016

Define-XML 2.1 (upcoming)

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 and ADaM standards and best practices. Key enhancements include:

- 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.

Define-XML v2.0 is the most current version of this standard and its use is recommended.

# SDTM/Define-XML Releases Background – Overview

## FDA SUPPORTED VERSION ON DATA STANDARDS



### FDA Data Standards Catalog v4.5 (07-18-2016) - Supported and Required Standards

This table contains a listing of the data exchange, file formats and terminology standards supported at FDA. These standards have gone through all the steps necessary to make this part of the regulatory review process, including posting of regulatory guidance documents and associated implementation guidelines and technical specifications. The submission of standardized data using any standard not listed, or to an FDA Center not listed, should be discussed with the Agency in advance. This catalog is incorporated by reference in the guidance to industry, *Providing Regulatory Submissions in Electronic format-Standardized Study Data* (<http://www.fda.gov/downloads/Drugs/Guidances/UCM292334.pdf>).

| Use                     | Data Exchange Standard                           | Exchange Format | Standards Development Organization (SDO)               | Supported Version | Implementation Guide Version | FDA Center(s)    | Date Support Begins (MM/DD/YYYY) | Date Support Ends (MM/DD/YYYY) | Date Requirement Begins (MM/DD/YYYY) | Date Requirement Ends | Regulatory Reference and Information Sources          |
|-------------------------|--------------------------------------------------|-----------------|--------------------------------------------------------|-------------------|------------------------------|------------------|----------------------------------|--------------------------------|--------------------------------------|-----------------------|-------------------------------------------------------|
| Clinical study datasets | Study Data Tabulation Model (SDTM)               | XPT             | Clinical Data Interchange Standards Consortium (CDISC) | 1.4               | 3.2                          | CDER, CBER       | 08/17/2015                       |                                | 03/15/2018 [1]<br>03/15/2019 [2]     |                       | <a href="http://CDISC.org">CDISC.org</a> - SDTM       |
|                         |                                                  |                 |                                                        |                   |                              |                  |                                  |                                |                                      |                       | <a href="#">See Technical Conformance Guide</a>       |
| Clinical study datasets | SDTM                                             | XPT             | CDISC                                                  | 1.3               | 3.1.3                        | CDER, CBER       | 12/01/2012                       |                                | 12/17/2016 [1]<br>12/17/2017 [2]     |                       | <a href="http://CDISC.org">CDISC.org</a> - SDTM       |
| Clinical study datasets | SDTM                                             | XPT             | CDISC                                                  | 1.2               | Version 3.1.2 Amendment 1    | CDER, CBER       | 08/07/2013                       |                                | 12/17/2016 [1]<br>12/17/2017 [2]     |                       | <a href="http://CDISC.org">CDISC.org</a> - SDTM       |
| Clinical study datasets | SDTM                                             | XPT             | CDISC                                                  | 1.2               | 3.1.2                        | CDER, CBER       | 10/30/2009                       |                                | 12/17/2016 [1]<br>12/17/2017 [2]     |                       | <a href="http://CDISC.org">CDISC.org</a> - SDTM       |
| Clinical study datasets | SDTM                                             | XPT             | CDISC                                                  | 1.1               | 3.1.1                        | CDER, CBER       | Ongoing                          | 01/28/2015                     |                                      |                       | <a href="http://CDISC.org">CDISC.org</a> - SDTM       |
| Clinical study datasets | Analysis Data Model (ADaM)                       | XPT             | CDISC                                                  | 2.1               | 1.0                          | CDER, CBER       | Ongoing                          |                                | 12/17/2016 [1]<br>12/17/2017 [2]     |                       | <a href="http://CDISC.org">CDISC.org</a> - ADaM       |
| Animal study datasets   | Standard for Exchange of Nonclinical Data (SEND) | XPT             | CDISC                                                  | 1.2               | 3.0                          | CDER             | 06/13/2011                       |                                | 12/17/2016 [1]<br>12/17/2017 [2]     |                       | <a href="http://CDISC.org">CDISC.org</a> - SEND       |
| Study data definition   | Define                                           | XML             | CDISC                                                  | 1.0               | N/A                          | CDER, CBER, CDRH | Ongoing                          | 03/17/2017                     | 12/17/2016 [1]<br>12/17/2017 [2]     |                       | <a href="http://CDISC.org">CDISC.org</a> - Define-XML |
| Study data definition   | Define                                           | XML             | CDISC                                                  | 2.0               | N/A                          | CDER, CBER, CDRH | 08/07/2013                       |                                | 12/17/2016 [1]<br>12/17/2017 [2]     |                       | <a href="http://CDISC.org">CDISC.org</a> - Define-XML |

The FDA has announced the end of support for Define-XML v1.0 for studies would be March, 2017.

This section is reserved for future therapeutic area data standards

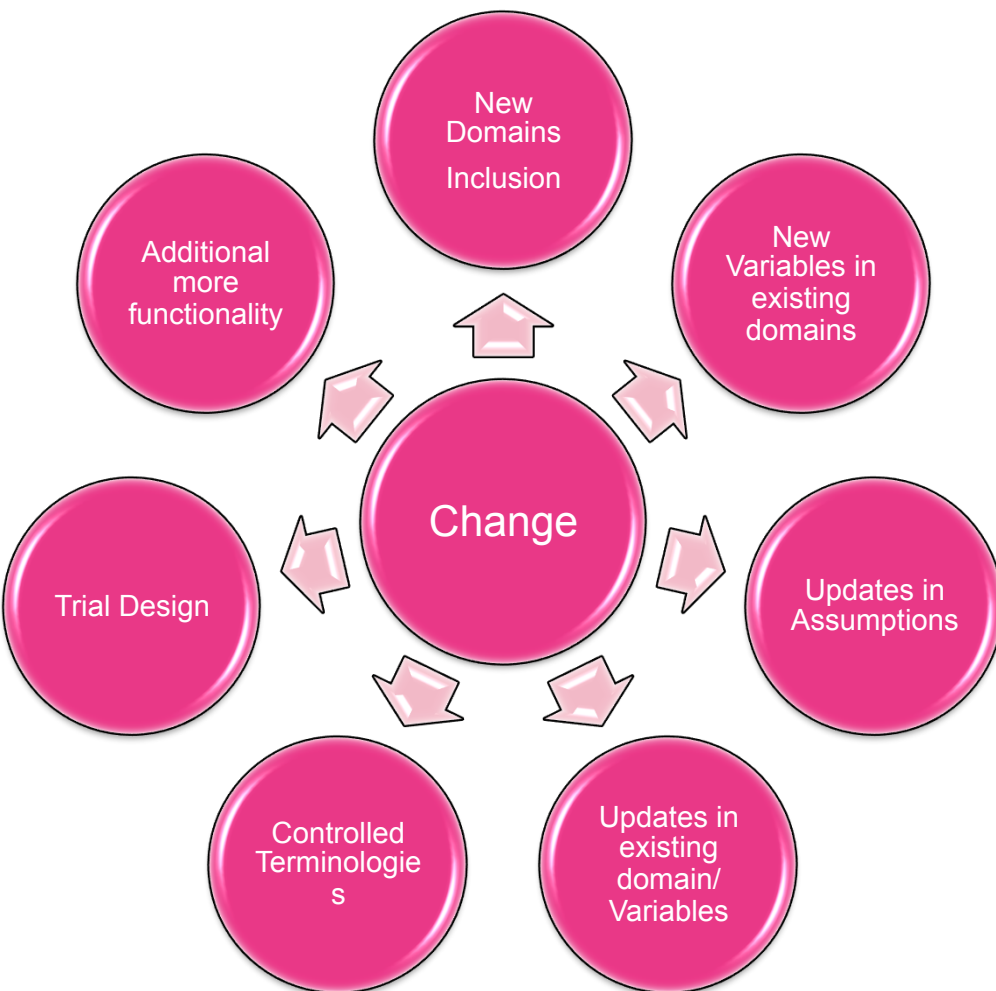
Download from : <http://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM340684.xlsx>



# Changes from One SDS to Another SDS Version

# Changes from One SDS to Another SDS Version

Generally CDISC published the following changes and it is classified as major and minor.



## 3.2 New Domains



- ☐ EC - Exposure as Collected
- ☐ PR - Procedures
- ☐ HO - Healthcare Encounters
- ☐ DD - Death Details
- ☐ IS - Immunogenicity Specimen Assessment
- ☐ MI - Microscopic Findings
- ☐ MO - Morphology
- ☐ RP - Reproductive System Findings
- ☐ SS - Subject Status
- ☐ SR - Skin Response
- ☐ TD - Trial Disease Assessments

## 3.3 New Domains



- ☐ ML - Meal Data
- ☐ CV - Cardiovascular System Findings
- ☐ ER - Environmental Risk Factors
- ☐ MK - Musculoskeletal System Findings
- ☐ NV - Nervous System Findings
- ☐ OE - Ophthalmic Examinations
- ☐ QT - ECG QT Correction Model Data
- ☐ RE - Respiratory System Findings
- ☐ UR - Urinary System Findings
- ☐ RELSUB - Related Subjects
- ☐ OI - Non-host Organism Identifiers

## 3.3 Revised Domains



- ☐ DM - Demographics
- ☐ CM - Concomitant/Prior Medications
- ☐ CE - Clinical Events
- ☐ MH - Medical History
- ☐ EG - ECG Test Results
- ☐ MB - Microbiology Specimen
- ☐ MS - Microbiology Susceptibility
- ☐ PE - Physical Exam
- ☐ RP - Reproductive System Findings
- ☐ RS - Disease Response and Clin Classification

# Changes from One SDS to Another SDS Version - Identification

Using CDISC eSHARE Downloads - (<http://www.cdisc.org/members-only/eshare-downloads>)



For quick identification of changes from one version to another version can be found in the eSHARE downloads members only area. For example, it contains around 171 changes from SDTM 3.1.3 to 3.2

| SDTM 1.4 (IG 3.2) |              |                |                 |                                                                                           |
|-------------------|--------------|----------------|-----------------|-------------------------------------------------------------------------------------------|
| 2015-02-02        | SDTM IG Diff | 3.2 - 3.1.3    | Metadata        | <a href="#">Excel</a>                                                                     |
| 2014-08-21        | SDTM IG      | 1.4 (3.2)      | Metadata        | <a href="#">Define-XML v2.0</a>   <a href="#">Define-XML v1.0</a>   <a href="#">Excel</a> |
| 2014-08-21        | SDTM + CT    | 1.4+2013-12-20 | Bundle          | <a href="#">Define-XML v2.0</a>   <a href="#">Excel</a>                                   |
| 2014-08-21        | SDTM IG      | 1.3 (3.1.3)    | Document Bundle | <a href="#">PDF</a>                                                                       |

Downloaded excel from the above table is shown. The downloaded excel contains changes made in the new version by identifying it as 'Add', 'Update', 'Remove'. Based on the information available, user would be able to identify the changes quickly and list the different type of work to be undertaken in output dataset creation and Define-XML file generation



| Change Nbr | Action    | Impact                      | Domain   | Variable | Attribute (updated)                                                                                                                                                                                                                                                                                                                                     | Attribute (previous)                                 | Updated SDTM-IG Ver | Previous SDTM-IG Ver |
|------------|-----------|-----------------------------|----------|----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|---------------------|----------------------|
| 1          | 0 Add     | Domain                      | APDM     |          |                                                                                                                                                                                                                                                                                                                                                         |                                                      |                     | 3.2 3.1.3            |
| 2          | 1 Add     | Domain                      | APRELSUB |          |                                                                                                                                                                                                                                                                                                                                                         |                                                      |                     | 3.2 3.1.3            |
| 3          |           |                             |          |          | Describes changes to the study treatment as a result of the event. AEACN is specifically for the relationship to study treatment. AEACNOTH is for actions unrelated to dose adjustments of study treatment. Examples of AEACN values include ICH E2B values: DRUG WITHDRAWN, DOSE REDUCED, DOSE INCREASED, DOSE NOT CHANGED, UNKNOWN or NOT APPLICABLE. | Describes changes to the study treatment as a        | 3.2 3.1.3           | 3.2 3.1.3            |
| 4          | 2 Update  | CDISC Notes and Definitions | AE       | AEACN    |                                                                                                                                                                                                                                                                                                                                                         |                                                      |                     | 3.2 3.1.3            |
| 5          | 3 Add     | Controlled Terminology      | AE       | AEDECOO  | MedDRA                                                                                                                                                                                                                                                                                                                                                  |                                                      |                     | 3.2 3.1.3            |
| 6          | 4 Update  | CDISC Notes and Definitions | AE       | AEDECOO  | Dictionary derived text description of AETERM or AEMODIFY. Equivalent to the Preferred Term (PT in MedDRA). The sponsor is expected to provide the dictionary name and version used to map the terms utilizing the define.xml external codelist attributes.                                                                                             | Dictionary derived text description of AETERM or     | 3.2 3.1.3           | 3.2 3.1.3            |
| 7          | 5 Update  | Controlled Terminology      | AE       | AEENRTP  | (STENRF)                                                                                                                                                                                                                                                                                                                                                | BEFORE, AFTER, COINCIDENT, ONGOING, U                |                     | 3.2 3.1.3            |
| 8          | 6 Update  | CDISC Notes and Definitions | AE       | AELOC    | Describes anatomical location relevant for the event (e.g., ARM for skin rash).                                                                                                                                                                                                                                                                         | Describes anatomical location relevant for the e     | 3.2 3.1.3           | 3.2 3.1.3            |
| 9          | 7 Update  | Role                        | AE       | AEPRSP   | Variable Qualifier                                                                                                                                                                                                                                                                                                                                      | Record Qualifier                                     |                     | 3.2 3.1.3            |
| 10         | 8 Update  | CDISC Notes and Definitions | AE       | AEREFID  | Internal or external identifier such as a serial number on an SAE reporting form.                                                                                                                                                                                                                                                                       | Internal or external identifier such as a serial num |                     | 3.2 3.1.3            |
| 11         | 9 Update  | CDISC Notes and Definitions | AE       | AEREL    | Records the investigators opinion as to the causality of the event to the treatment. ICH E2A and E2B examples include NOT RELATED, UNLIKELY RELATED, POSSIBLY RELATED, RELATED. Controlled Terminology may be defined in the future. Check with regulatory authority for population of this                                                             | Records the investigators opinion as to the caus     | 3.2 3.1.3           |                      |
| 12         | 10 Update | CDISC Notes and Definitions | AE       | AETOXGR  | Toxicity grade according to a standard toxicity scale such as Common Terminology Criteria for Adverse Events v3.0 (CTCAE). Sponsor should specify name of the scale and version used in the metadata (see Assumption 6d). If value is from a numeric scale, represent only the number (e.g., 2 and                                                      | Toxicity grade according to a standard toxicity s    | 3.2 3.1.3           | 3.2 3.1.3            |
| 13         | 11 Update | Controlled Terminology      | CE       | CEENRTP  | (STENRF)                                                                                                                                                                                                                                                                                                                                                | BEFORE, AFTER, COINCIDENT, ONGOING, U                |                     | 3.2 3.1.3            |
| 14         | 12 Update | Role                        | CE       | CEPRSP   | Variable Qualifier                                                                                                                                                                                                                                                                                                                                      | Record Qualifier                                     |                     | 3.2 3.1.3            |
| 15         | 13 Update | Controlled Terminology      | CE       | CESTRTP  | (STENRF)                                                                                                                                                                                                                                                                                                                                                | BEFORE, AFTER, COINCIDENT, U                         |                     | 3.2 3.1.3            |
| 16         | 14 Add    | Controlled Terminology      | DS       | EPOCH    | (EPOCH)                                                                                                                                                                                                                                                                                                                                                 |                                                      |                     | 3.2 3.1.3            |
| 17         | 15 Update | CDISC Notes and Definitions | DS       | EPOCH    | EPOCH may be used when DSCAT = DISPOSITION EVENT. Examples: SCREENING, TREATMENT, FOLLOWUP                                                                                                                                                                                                                                                              | EPOCH may be used when DSCAT = DISPOSITI             | 3.2 3.1.3           | 3.2 3.1.3            |
| 18         | 16 Add    | Controlled Terminology      | DV       | EPOCH    | (EPOCH)                                                                                                                                                                                                                                                                                                                                                 |                                                      |                     | 3.2 3.1.3            |
| 19         | 17 Add    | Domain                      | HO       |          |                                                                                                                                                                                                                                                                                                                                                         |                                                      |                     | 3.2 3.1.3            |
| 20         | 18 Update | CDISC Notes and Definitions | MH       | MHDECOO  | Dictionary derived text description of MHTERM or MHMODIFY. Equivalent to the Preferred Term (PT in MedDRA). The sponsor is expected to provide the dictionary name and version used to map the terms utilizing the define.xml external codelist attributes.                                                                                             | Dictionary derived text description of MHTERM or     | 3.2 3.1.3           | 3.2 3.1.3            |
| 21         | 19 Update | Controlled Terminology      | MH       | MHENRTP  | (ENRTP)                                                                                                                                                                                                                                                                                                                                                 | BEFORE, AFTER, COINCIDENT, ONGOING, U                |                     | 3.2 3.1.3            |
| 22         | 20 Update | Role                        | MH       | MHPRES   | Variable Qualifier of --TERM                                                                                                                                                                                                                                                                                                                            | Record Qualifier                                     |                     | 3.2 3.1.3            |
| 23         | 21 Update | Variable Label              | MH       | MHREASND | Reason Medical History Not Done or Not Occurred                                                                                                                                                                                                                                                                                                         | Reason Medical History Not Collected                 |                     | 3.2 3.1.3            |

# Changes from One SDS to Another SDS Version - Identification

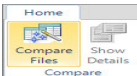
## Office 2013 Spreadsheet Compare Tool



1. Download SDTM IG metadata excel spreadsheet from eSHARE page. By this, two different excel file is downloaded namely, SDTM 3.1.3 and SDTM 3.2 metadata sheets.

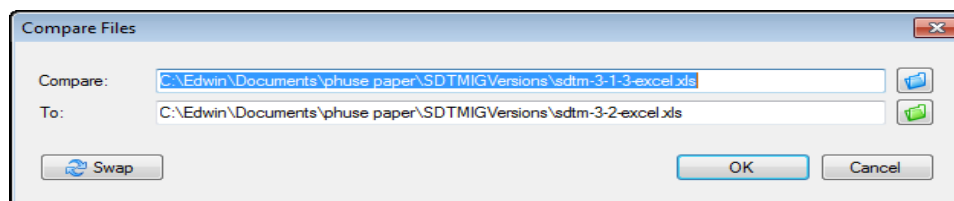
|                            |              |                |                 |                                                                                         |
|----------------------------|--------------|----------------|-----------------|-----------------------------------------------------------------------------------------|
| <b>SDTM 1.4 (IG 3.2)</b>   |              |                |                 |                                                                                         |
| 2015-02-02                 | SDTM IG Diff | 3.2 - 3.1.3    | Metadata        | <a href="#">Excel</a>                                                                   |
| 2014-08-21                 | SDTM IG      | 1.4 (3.2)      | Metadata        | <a href="#">Define-XML v2.0</a>   <a href="#">Define-XML v1.0</a> <a href="#">Excel</a> |
| 2014-08-21                 | SDTM + CT    | 1.4+2013-12-20 | Bundle          | <a href="#">Define-XML v2.0</a>   <a href="#">Excel</a>                                 |
| 2014-08-21                 | SDTM IG      | 1.3 (3.1.3)    | Document Bundle | <a href="#">PDF</a>                                                                     |
| <b>SDTM 1.3 (IG 3.1.3)</b> |              |                |                 |                                                                                         |
| 2014-08-21                 | SDTM IG      | 1.3 (3.1.3)    | Metadata        | <a href="#">Define-XML v2.0</a>   <a href="#">Define-XML v1.0</a> <a href="#">Excel</a> |
| 2014-08-21                 | SDTM + CT    | 1.3+2013-12-20 | Bundle          | <a href="#">Define-XML v2.0</a>   <a href="#">Excel</a>                                 |
| 2014-08-21                 | SDTM IG      | 1.3 (3.1.3)    | Document Bundle | <a href="#">PDF</a>                                                                     |

2. Open Spreadsheet Compare → In Start menu, go to Office 2013 Tools, and click Spreadsheet Compare.

3. Click Home → Compare Files.  Compare Files dialog box appears.

4. Click the blue folder icon next to the Compare box to browse the location of older SDTM version. In addition to files saved locally on your computer, it is possible to compare files on a network

5. Click the green folder icon next to the 'To' box to browse the location of the workbook that you want to compare to the earlier version, and then click OK.



6. In the left pane, choose the compare options you want to see in the results of the workbook comparison by checking or unchecking the options, such as Formulas, Macros, or Cell Format. Or, just Select All.

7. Click Ok to run the comparison.

# Changes from One SDS to Another SDS Version - Identification

## Office 2013 Spreadsheet Compare Tool

The screenshot displays the Microsoft Office Spreadsheet Compare tool interface. The top ribbon includes tabs for Home, Compare, Show Details, Show Formulas, Show Workbook Formatting, Export Results, Copy Results to Clipboard, Options, and Help. The main window shows a comparison between two Excel files: [sdtm-3-1-3-excel.xls] and [sdtm-3-2-excel.xls].

The comparison results are shown in a table with columns A through K. The table lists various data points and their corresponding roles. A specific change is highlighted with a red box and a callout: **CE.CEPRESP (Role: Record Qualifier)** in the first file and **CE.CEPRESP (Role: Variable Qualifier)** in the second file.

Below the main table, there is a section for 'Enable Option' with checkboxes for various options like 'Select All', 'Entered Values', 'Calculated Values', 'Formulas', 'SysGen Formulas', 'Structural', 'Names', 'SysGen Names', 'Data Connection', 'Cell Format', and 'Cell Protection'. A 'Change Description' table is also visible, showing the details of the changes.

On the right side, a bar chart displays the count of various changes. The chart shows the following counts:

| Change Type              | Count |
|--------------------------|-------|
| Entered Values           | 120   |
| Calculated Values        | 10    |
| Formulas                 | 5     |
| SysGen Formulas          | 2     |
| SysGen Formulas (Errors) | 1     |
| Structural               | 1     |
| Names                    | 1     |
| SysGen Names             | 1     |
| SysGen Names (Errors)    | 1     |
| Macros                   | 1     |
| Data Connections         | 1     |
| Cell Formats             | 1     |
| Cell Protections         | 1     |
| Workbook Protection      | 1     |

In the above example shown, results for domain CE.CEPRESP variable role changed from Record Qualifier to Variable Qualifier in the SDTM 3.2 version.

If the compare tool does not provide the accurate result across all domains, then split the excel file domain-wise and compare it.

# Changes from One SDS to Another SDS Version - Identification

## SAS Program or Macro

SAS programmer is to develop a macro to compare two versions and display the differences in a customized report form. The report will present the following:

- Display all the newly added domains
- Display all the variables assigned for the newly added domains
- Display all the variables names in which added into the existing domains
- Display all the deleted variables from the existing domains
- Display all the variables names in which attributes updated

Below is a simple SAS code for listing the added and deleted details from two versions. This example uses the eSHARE metadata excel files as an input.

```
*** Import SDTM IG 3.1.3 version;
libname sdtm "C:\Edwin\Documents\phuse paper\SDTMIGVersions";
proc import datafile="C:\Edwin\Documents\phuse paper
\SDTMIGVersions\sdtm-3-1-3-excel.xls" out=sdtm.sdtm313 dbms=xls
replace;
run;
quit;
```

```
*** Import SDTM IG 3.2 version;
libname sdtm "C:\Edwin\Documents\phuse paper\SDTMIGVersions
\sdtm-3-1-3";
proc import datafile="C:\Edwin\Documents\phuse paper
\SDTMIGVersions\sdtm-3-2-excel.xls" out=sdtm.sdtm32 dbms=xls
replace;
run;
quit;
```

```
*** Sorting by domain and variables;
proc sort data=sdtm.sdtm313 out=sdtm313 nodup;
      by Domain_Prefix Variable_Name;
run;

proc sort data=sdtm.sdtm32 out=sdtm32 nodup;
      by Domain_Prefix Variable_Name;
run;

*** To find the list of new variables added [in
tdnew] and deleted [in tdold] in the SDTM IG
Versions;
data tdnew tdold ;
      merge sdtm32(in=nw) sdtm313(in=od);
      by Domain_Prefix Variable_Name;
      if nw & not(od) then output tdnew;
      else if od & not(nw) then output tdold;
run;

proc sort data=tdnew out=tdnew;
      by Domain_Prefix Seq__For_Order
Variable_Name;
run;

proc sort data=tdold out=tdold;
      by Domain_Prefix Seq__For_Order
Variable_Name;
run;

*** Export the output details in to excel;
proc export data=tdnew outfile="C:\Edwin\Documents
\phuse paper\SDTMIGVersions\Added.xls" dbms=xls
replace;
run;
quit;

proc export data=tdold outfile="C:\Edwin\Documents
\phuse paper\SDTMIGVersions\Deleted.xls" dbms=xls
replace;
run;
quit;
```





# Problem Statement

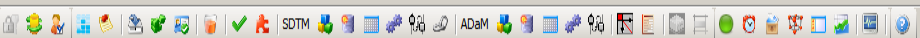
A Study starts with initial prerequisite items filled up under the advice of the Sponsor, which includes the adoption of SDS version for the submission. During the course of the study, there can be changes initiated by FDA or Sponsor themselves would request the study team to make amendments to submission plan by requesting to work on a different SDS version for submission. Such situations would occur in late phase trials where the study duration exceeds a month. At times, it would impact early phase trials which run for few weeks.

Under such circumstances, the study team would have to make amendments for the ongoing study which would have been started, configured and even output created in one version to a different version. The amendment varies from output dataset handling to Define-XML creation.

Going forward, this paper would be taking up a case where the SDS version changes from v3.1.3 to v3.2 and Define-XML changes from v1.0 to v2.0 for an ongoing study



The Solution is...



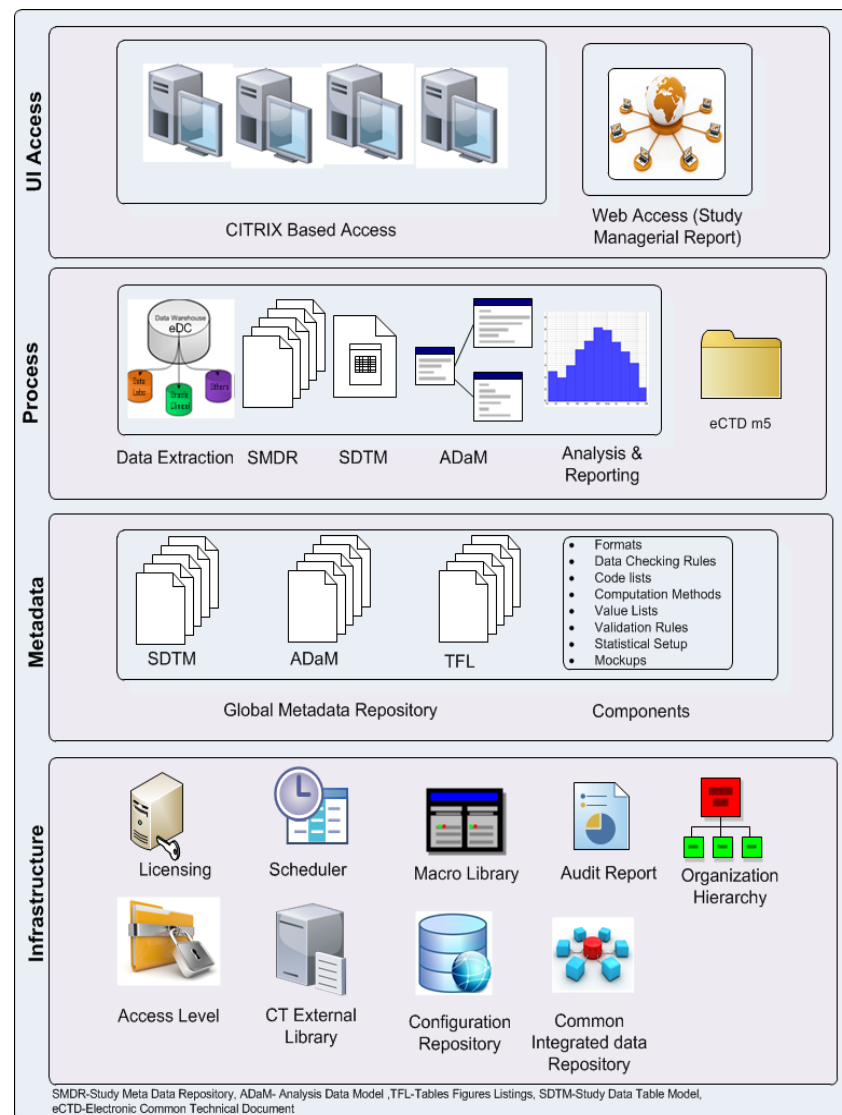
# EXACT™



Many solutions were discussed in earlier section to perform a compare of versions and then, proceed manually to implement the changes and rerun the program set. This paper deals with a semi-automated approach with a demonstration outlining the approach & process to make the change with ease and still maintain the quality in less time. Proposed demonstration is done using an enterprise class system: EXACT.

**EX**traction, **A**nalysis, **C**onversion and **T**abulation (EXACT) is an outcome of integrating clinical and non-clinical data from multiple sources into a single environment where it can be standardized, analyzed, visualized and reported on by clinical researchers to regulatory agencies in shorter span of time from last observation last visit.

EXACT brings a complete set of process automation using the implementation of Clinical Meta Data Repository model across different stages of clinical development by enabling the user to extract, view, transform, analyze and report data across clinical applications, and across projects or trials in different therapeutics within the same environment and in a regulatory compliant manner. This is achieved in EXACT by extracting data from various sources that are available for a study and creating a fully controlled, traceable, full GCP and 21 CFR Part 11 compliant data for various analyses & within modules that are integrated in the product.



# Manage CDISC Metadata & Sponsor Metadata

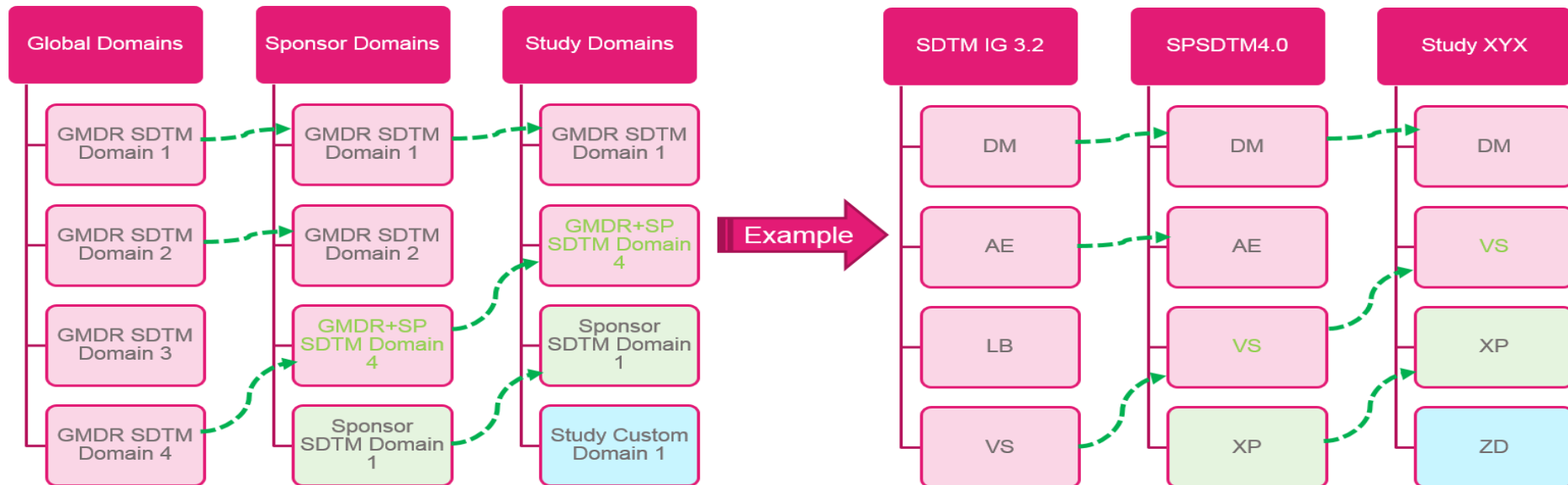
## In EXACT



EXACT™ stores and manage all the CDISC published metadata, sponsor metadata with additional attributes which requires for the SDTM dataset and Define-XML generation into its repository. If any new SDTM IG version released by CDISC or Sponsor, it can be easily imported into the system if there is no structural changes. These metadata details will be re-used under each study based on the SDTM IG or Sponsor version. These metadata is stored under EXACT Administrator module and managed by the standards group and the standards librarian within our organization.

Below diagram shows how metadata will be inherited from the global level to below levels namely, sponsor, study.

Metadata flow from Global-Sponsor-Study



# Manage CDISC Metadata & Sponsor Metadata In EXACT



Kinship EXACT Administrator

Welcome, Edwin Thangarajan

File Edit View System Administration Global Library Manager Sponsor Library Manager Study Manager Reports Help

Global Sponsor

Manage Metadata (GMDR)

Type: CDISC SDTM V 3.2

Class: Select

Domain: CDISC SDTM V 3.1.2, CDISC SDTM V 3.1.3, **CDISC SDTM V 3.2**, CDISC SDTM MD V 1.0, CDISC ADaM V 2.1, Analysis & Reporting

Classes and Domains

- Trial Design Domains
  - TA (Trial Arms)
  - TD (Trial Disease Assessment)
  - TE (Trial Elements)
  - TI (Trial Inclusion/Exclusion Criteria)
  - TS (Trial Summary)
  - TV (Trial Visits)
  - TX (Trial Sets)
- Special-Purpose Domains
  - CO (Comments)
  - DM (Demographics)**
  - SE (Subject Elements)
  - SV (Subject Visits)
- Interventions General Observation Class
- Events General Observation Class
  - AE (Adverse Events)
  - CE (Clinical Events)
  - DS (Disposition)
  - DV (Protocol Deviations)
  - HO (Healthcare Encounters)
  - MH (Medical History)
- Findings General Observation Class
- Findings About
- Relationship Datasets
- Others
- Associated Persons
  - APDM (Associated Persons Demographics)
  - APRELSUB (Associated Persons Related to Subjects)

View Domain Details

Domain Name: DM Domain Label: Demographics

Class Name: Special-Purpose Domains

Structure: One record per subject

Purpose: Tabulation ☐ Is Repeat Data ☐ Is Reference Data

Key Variables: STUDYID, USUBJID

SEQ Generation Based On: None

Domain Variables

| Variable Name | Data Type | Variable Label                     | Type         | Order |
|---------------|-----------|------------------------------------|--------------|-------|
| STUDYID       | Character | Study Identifier                   | User Defined | 1     |
| DOMAIN        | Character | Domain Abbreviation                | User Defined | 2     |
| USUBJID       | Character | Unique Subject Identifier          | User Defined | 3     |
| SUBJID        | Character | Subject Identifier for the Study   | User Defined | 4     |
| RFSTDTC       | Character | Subject Reference Start Date/Time  | User Defined | 5     |
| RFENDTC       | Character | Subject Reference End Date/Time    | User Defined | 6     |
| RFXSTDTC      | Character | Date/Time of First Study Treatment | User Defined | 7     |
| RFXENDTC      | Character | Date/Time of Last Study Treatment  | User Defined | 8     |

View Variable Details

Variable Name: STUDYID

Variable Label: Study Identifier

Variable Type: None

Variable Role: Identifier

Variable Core: Required

ODM Data Type: Text

Variable Origin: ☐ CRF ☐ Derived ☐ CRF Page ☐ eDT

For Help, press F1 Environment: Delivery NUM Version: v6.2.0.23

The following SDTM versions are currently available and loaded into EXACT.

- SDTM IG 3.1.1 (outdated)
- SDTM IG 3.1.2
- SDTM IG 3.1.3
- SDTM IG 3.2
- SDTM IG AP 1.0
- SDTM IG Medical Devices 1.0
- SDTM Terminologies



# Handling SDTM One Version to Another in a Study

This section of the presentation provides the necessary approach & steps that need to be followed in a semi-automated fashion to change from one SDS IG version 3.1.3 to v3.2. It is understood that EXACT has both the versions that is required for the ongoing study and one of the version has been used for generating the output dataset. But, with the current change in requirement, it is required to generate the output SDTM dataset in a new version.

- New Domain Inclusion
- New Variables and Updates in the Existing Domain/Variables

# Handling SDTM One Version to Another in a Study

## New Domain Inclusion



The screenshot shows the CDISC SDTM Domain Level Metadata (DLM) interface. On the left, under 'Standard CDISC Domains', the 'Interventions General Observation Class' is expanded, and 'EX (Exposure as Collected)' is highlighted with a red dashed box. A red arrow points from this box to the 'Study CDISC Domains' panel on the right, where 'EX (Exposure as Collected)' is also highlighted with a red dashed box. Below these panels, the 'Class Name' is set to 'Interventions General Observation Class', 'Domain Name' is 'EC', 'Domain Label' is 'Exposure as Collected', and 'Purpose' is 'Tabulation'. The 'Key Variables' field contains 'STUDYID, USUBJID, ECTRT, ECSTDTC'. A red arrow points from the 'EX (Exposure as Collected)' domain in the 'Study CDISC Domains' panel to the 'Variable Level Metadata' table in the screenshot below.

EXACT has the feature in Domain Level Metadata (DLM) UI to move the domains from CDISC/Sponsor repository to study level which in turns makes all the metadata available for the study. Variable Level Metadata (VLM) UI is shown to display all the variables post move from Sponsor to Study using DLM UI.

The screenshot shows the CDISC SDTM Variable Level Metadata (VLM) interface. The table displays variables for 'PRA Study 001' across various domains. The table has columns for Study Name, Domain Name, Variable Order, Variable Name, Variable Data Type, Variable Label, Key, Variable Core, Variable Role, Role, Other, Include Role, Variable Length, Variable Display Format, ODM Data Type, Significant Digits, and Variable Origin.

|     | Study Name    | Domain Name | Variable Order | Variable Name | Variable Data Type | Variable Label                  | Key | Variable Core | Variable Role      | Role, Other | Include Role             | Variable Length | Variable Display Format | ODM Data Type | Significant Digits | Variable Origin |
|-----|---------------|-------------|----------------|---------------|--------------------|---------------------------------|-----|---------------|--------------------|-------------|--------------------------|-----------------|-------------------------|---------------|--------------------|-----------------|
| 172 | PRA Study 001 | EC          | 1              | STUDYID       | Character          | Study Identifier                | 1   | Required      | Identifier         |             | <input type="checkbox"/> | 200             |                         | text          |                    | Derived         |
| 173 | PRA Study 001 | EC          | 2              | DOMAIN        | Character          | Domain Abbreviation             |     | Required      | Identifier         |             | <input type="checkbox"/> | 2               |                         | text          |                    | Assigned        |
| 174 | PRA Study 001 | EC          | 3              | USUBJID       | Character          | Unique Subject Identifier       | 2   | Required      | Identifier         |             | <input type="checkbox"/> | 200             |                         | text          |                    | Derived         |
| 175 | PRA Study 001 | EC          | 4              | ECSEQ         | Numeric            | Sequence Number                 |     | Required      | Identifier         |             | <input type="checkbox"/> | 8               |                         | integer       |                    | Derived         |
| 176 | PRA Study 001 | EC          | 5              | ECGRPID       | Character          | Group ID                        |     | Permissible   | Identifier         |             | <input type="checkbox"/> | 15              |                         | text          |                    | Assigned        |
| 177 | PRA Study 001 | EC          | 6              | ECREFID       | Character          | Reference ID                    |     | Permissible   | Identifier         |             | <input type="checkbox"/> | 25              |                         | text          |                    | Assigned        |
| 178 | PRA Study 001 | EC          | 7              | ECSPID        | Character          | Sponsor-Defined Identifier      |     | Permissible   | Identifier         |             | <input type="checkbox"/> | 15              |                         | text          |                    | CRF Page        |
| 179 | PRA Study 001 | EC          | 8              | ECLNKID       | Character          | Link ID                         |     | Permissible   | Identifier         |             | <input type="checkbox"/> | 25              |                         | text          |                    | Assigned        |
| 180 | PRA Study 001 | EC          | 9              | ECLNKGRP      | Character          | Link Group ID                   |     | Permissible   | Identifier         |             | <input type="checkbox"/> | 25              |                         | text          |                    | Assigned        |
| 181 | PRA Study 001 | EC          | 10             | ECTRT         | Character          | Name of Treatment               | 3   | Required      | Topic              |             | <input type="checkbox"/> | 200             |                         | text          |                    | CRF Page        |
| 182 | PRA Study 001 | EC          | 11             | ECMOOD        | Character          | Mood                            |     | Permissible   | Record Qualifier   |             | <input type="checkbox"/> | 200             |                         | text          |                    | Assigned        |
| 183 | PRA Study 001 | EC          | 12             | ECCAT         | Character          | Category of Treatment           |     | Permissible   | Grouping Qualifier |             | <input type="checkbox"/> | 200             |                         | text          |                    | CRF Page        |
| 184 | PRA Study 001 | EC          | 13             | ECSCAT        | Character          | Subcategory of Treatment        |     | Permissible   | Grouping Qualifier |             | <input type="checkbox"/> | 200             |                         | text          |                    | CRF Page        |
| 185 | PRA Study 001 | EC          | 14             | ECPRES        | Character          | Pre-Specified                   |     | Permissible   | Record Qualifier   |             | <input type="checkbox"/> | 1               |                         | text          |                    | CRF Page        |
| 186 | PRA Study 001 | EC          | 15             | ECOCUR        | Character          | Occurrence                      |     | Permissible   | Record Qualifier   |             | <input type="checkbox"/> | 1               |                         | text          |                    | CRF Page        |
| 187 | PRA Study 001 | EC          | 16             | ECDOSE        | Numeric            | Dose                            |     | Expected      | Record Qualifier   |             | <input type="checkbox"/> | 8               |                         | integer       |                    | CRF Page        |
| 188 | PRA Study 001 | EC          | 17             | ECDOSTXT      | Character          | Dose Description                |     | Permissible   | Record Qualifier   |             | <input type="checkbox"/> | 200             |                         | text          |                    | CRF Page        |
| 189 | PRA Study 001 | EC          | 18             | ECDOSU        | Character          | Dose Units                      |     | Expected      | Variable Qualifier |             | <input type="checkbox"/> | 25              |                         | text          |                    | CRF Page        |
| 190 | PRA Study 001 | EC          | 19             | ECDOSFRM      | Character          | Dose Form                       |     | Expected      | Variable Qualifier |             | <input type="checkbox"/> | 200             |                         | text          |                    | CRF Page        |
| 191 | PRA Study 001 | EC          | 20             | ECDOSFRQ      | Character          | Dosing Frequency per Interval   |     | Permissible   | Variable Qualifier |             | <input type="checkbox"/> | 200             |                         | text          |                    | CRF Page        |
| 192 | PRA Study 001 | EC          | 21             | ECDOSTOT      | Character          | Total Daily Dose                |     | Permissible   | Record Qualifier   |             | <input type="checkbox"/> | 200             |                         | text          |                    | CRF Page        |
| 193 | PRA Study 001 | EC          | 22             | ECDOSRGM      | Character          | Intended Dose Regimen           |     | Permissible   | Variable Qualifier |             | <input type="checkbox"/> | 200             |                         | text          |                    | CRF Page        |
| 194 | PRA Study 001 | EC          | 23             | ECROUTE       | Character          | Route of Administration         |     | Permissible   | Variable Qualifier |             | <input type="checkbox"/> | 200             |                         | text          |                    | CRF Page        |
| 195 | PRA Study 001 | EC          | 24             | ECLOT         | Character          | Lot Number                      |     | Permissible   | Record Qualifier   |             | <input type="checkbox"/> | 50              |                         | text          |                    | CRF Page        |
| 196 | PRA Study 001 | EC          | 25             | ECLOC         | Character          | Location of Dose Administration |     | Permissible   | Record Qualifier   |             | <input type="checkbox"/> | 100             |                         | text          |                    | CRF Page        |
| 197 | PRA Study 001 | EC          | 26             | ECLAT         | Character          | Laterality                      |     | Permissible   | Record Qualifier   |             | <input type="checkbox"/> | 50              |                         | text          |                    | CRF Page        |

# Handling SDTM One Version to Another in a Study

## NEW VARIABLES AND UPDATES IN THE EXISTING DOMAIN/VARIABLES



EXACT has the feature to export the existing configured domain metadata and mapping definitions as excel spreadsheet and make necessary modifications and re-import quickly without changing the unchanged metadata and mapping definitions.

Export EX domain [3.1.3 version]

|   | A             | B                          | C             | D                  | E           | F                  | G               | H                     |
|---|---------------|----------------------------|---------------|--------------------|-------------|--------------------|-----------------|-----------------------|
|   | Variable Name | Variable Label             | Variable Core | Variable Role      | Role, Other | Variable Data Type | Variable Length | Variable Display Form |
| 1 | STUDYID       | Study Identifier           | Required      | Identifier         |             | Character          | 16              |                       |
| 2 | DOMAIN        | Domain Abbreviation        | Required      | Identifier         |             | Character          | 2               |                       |
| 3 | USUBJID       | Unique Subject Identifier  | Required      | Identifier         |             | Character          | 21              |                       |
| 4 | EXSEQ         | Sequence Number            | Required      | Identifier         |             | Numeric            | 8               |                       |
| 5 | EXGRPID       | Group ID                   | Permissible   | Identifier         |             | Character          | 15              |                       |
| 6 | EXSPID        | Sponsor-Defined Identifier | Permissible   | Identifier         |             | Character          | 15              |                       |
| 7 | EXTRT         | Name of Actual Treatment   | Required      | Topic              |             | Character          | 200             |                       |
| 8 | EXCAT         | Category for Treatment     | Permissible   | Grouping Qualifier |             | Character          | 200             |                       |
| 9 | EXSCAT        | Subcategory for Treatment  | Permissible   | Grouping Qualifier |             | Character          | 200             |                       |

- Make necessary changes to the exported metadata (add/modify) in the spreadsheet for the SDTM 3.2 usage for a study or use the SDTM 3.2 metadata sheet (Example: v3.2 EX variables 'EXLNKID', 'EXLNKGP' to be added )
- Select Import / Re Import option to re-import the specific domain

# Handling SDTM One Version to Another in a Study

## NEW VARIABLES AND UPDATES IN THE EXISTING DOMAIN/VARIABLES



- The export feature can be done for a single domain or more than one domain and the same can be reimported for a study. While doing the above steps, it would cover the variable level changes such as new variables or dropping of variables or change in attributes of a variable.
- Further to this, changes associated with inclusion of new variable would involve mapping configuration changes. This is done either through the exported sheet which contains the mapping information or post re-import by way of accessing the mapping user interface and make necessary configurations.

|     | Study Name    | Domain Name | Variable Order | Variable Name | Variable Data Type | Variable Label                  | Key | Variable Core | Variable Role      |
|-----|---------------|-------------|----------------|---------------|--------------------|---------------------------------|-----|---------------|--------------------|
| 172 | PRA Study 001 | EX          | 1              | STUDYID       | Character          | Study Identifier                | 1   | Required      | Identifier         |
| 173 | PRA Study 001 | EX          | 2              | DOMAIN        | Character          | Domain Abbreviation             |     | Required      | Identifier         |
| 174 | PRA Study 001 | EX          | 3              | USUBJID       | Character          | Unique Subject Identifier       | 2   | Required      | Identifier         |
| 175 | PRA Study 001 | EX          | 4              | EXSEQ         | Numeric            | Sequence Number                 |     | Required      | Identifier         |
| 176 | PRA Study 001 | EX          | 5              | EXGRPID       | Character          | Group ID                        |     | Permissible   | Identifier         |
| 177 | PRA Study 001 | EX          | 6              | EXREFID       | Character          | Reference ID                    |     | Permissible   | Identifier         |
| 178 | PRA Study 001 | EX          | 7              | EXSPID        | Character          | Sponsor-Defined Identifier      |     | Permissible   | Identifier         |
| 179 | PRA Study 001 | EX          | 8              | EXLNKID       | Character          | Link ID                         |     | Permissible   | Identifier         |
| 180 | PRA Study 001 | EX          | 9              | EXLNKGRP      | Character          | Link Group ID                   |     | Permissible   | Identifier         |
| 181 | PRA Study 001 | EX          | 10             | EXTRT         | Character          | Name of Treatment               | 3   | Required      | Topic              |
| 182 | PRA Study 001 | EX          | 11             | EXCAT         | Character          | Category of Treatment           |     | Permissible   | Grouping Qualifier |
| 183 | PRA Study 001 | EX          | 12             | EXSCAT        | Character          | Subcategory of Treatment        |     | Permissible   | Grouping Qualifier |
| 184 | PRA Study 001 | EX          | 13             | EXDOSE        | Numeric            | Dose                            |     | Expected      | Record Qualifier   |
| 185 | PRA Study 001 | EX          | 14             | EXDOSTXT      | Character          | Dose Description                |     | Permissible   | Record Qualifier   |
| 186 | PRA Study 001 | EX          | 15             | EXDOSU        | Character          | Dose Units                      |     | Expected      | Variable Qualifier |
| 187 | PRA Study 001 | EX          | 16             | EXDOSFRM      | Character          | Dose Form                       |     | Expected      | Variable Qualifier |
| 188 | PRA Study 001 | EX          | 17             | EXDOSFRQ      | Character          | Dosing Frequency per Interval   |     | Permissible   | Variable Qualifier |
| 189 | PRA Study 001 | EX          | 18             | EXDOSRGM      | Character          | Intended Dose Regimen           |     | Permissible   | Variable Qualifier |
| 190 | PRA Study 001 | EX          | 19             | EXROUTE       | Character          | Route of Administration         |     | Permissible   | Variable Qualifier |
| 191 | PRA Study 001 | EX          | 20             | EXLOT         | Character          | Lot Number                      |     | Permissible   | Record Qualifier   |
| 192 | PRA Study 001 | EX          | 21             | EXLOC         | Character          | Location of Dose Administration |     | Permissible   | Record Qualifier   |
| 193 | PRA Study 001 | EX          | 22             | EXLAT         | Character          | Laterality                      |     | Permissible   | Variable Qualifier |
| 194 | PRA Study 001 | EX          | 23             | EXDIR         | Character          | Directionality                  |     | Permissible   | Variable Qualifier |
| 195 | PRA Study 001 | EX          | 24             | EXFAST        | Character          | Fasting Status                  |     | Permissible   | Record Qualifier   |
| 196 | PRA Study 001 | EX          | 25             | EXADJ         | Character          | Reason for Dose Adjustment      |     | Permissible   | Record Qualifier   |
| 197 | PRA Study 001 | EX          | 26             | EPOCH         | Character          | Epoch                           |     | Permissible   | Timing             |



# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study

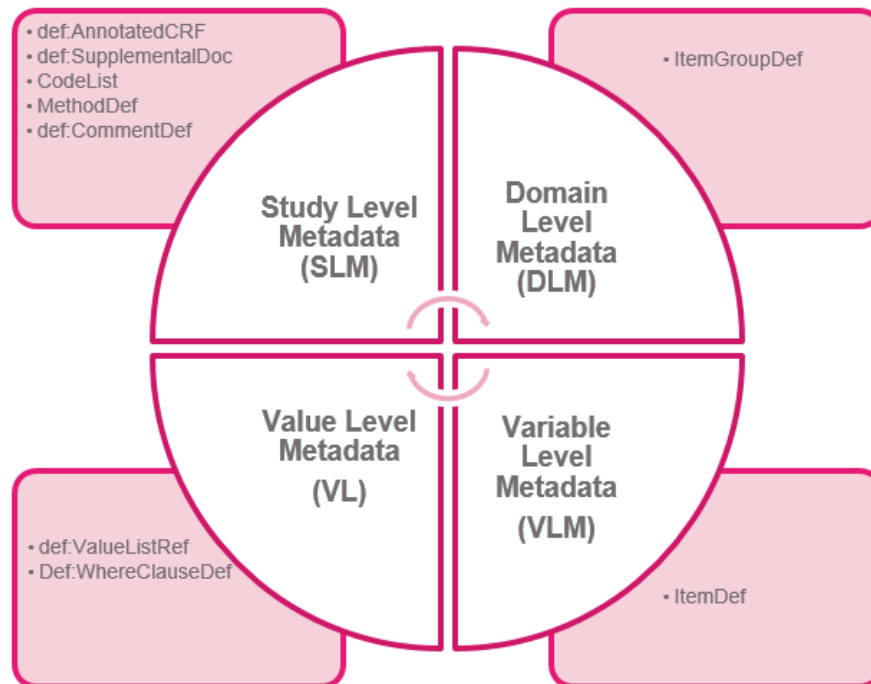
# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study

## In EXACT



It is informed by FDA that the end of support for Define-XML v1.0 for studies is March, 2017. In such case, most of the sponsor studies which were ongoing with Define-XML v1.0 has to plan for migration to Define-XML v2.0 based on the study duration. This situation is easily handled through the system to generate output datasets and define.xml file generation in the new version recommended.

The below data flow diagram represents the user interfaces and how the data flows to define file sections.



```
<?xml version="1.0" encoding="UTF-8"?>
<ODM xmlns="http://www.cdisc.org/ns/odm/v1.3"
  xmlns:xlink="http://www.w3.org/1999/xlink"
  xmlns:def="http://www.cdisc.org/ns/def/v2.0"
  FileType="Snapshot" ODMVersion="1.3.2"
  FileOID="Studydisc01-Define-XML_2.0.0"
  CreationDateTime="2012-06-21T11:07:23-05:00"
  Originator="CDISC XML Technologies Team">
  <Study OID="cdisc01">
    <GlobalVariables>
      <StudyName>CDISC01</StudyName>
      <StudyDescription>CDISC Test Study</StudyDescription>
      <ProtocolName>CDISC 01</ProtocolName>
    </GlobalVariables>
    <MetaDataVersion OID="MDV.CDISC01.SDTMIG.3.1.2.SDTM.1.2"
      Name="Study CDISC01, Data Definitions"
      Description="Study CDISC01, Data Definitions"
      def:DefineVersion="2.0.0"
      def:StandardName="CDISC SDTM"
      def:StandardVersion="3.1.2">
```

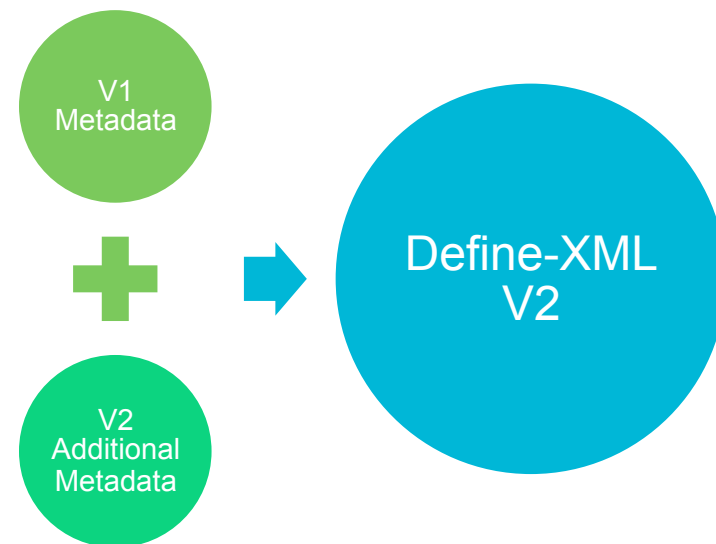
```
< Annotated Case Report Forms (def:AnnotatedCRF) >
< Supplemental Data Definitions (def:SupplementalDoc) >
< Value Level Metadata (def:ValueListDef) >
< Where Clause Definitions (def:WhereClauseDef) >
< Domain Level Metadata (ItemDef) >
< Variable Level Metadata (ItemDef) >
< Controlled Terminology Metadata (CodeList) >
< Computational Algorithms (MethodDef) >
< Comments (def:CommentDef) >
< Referenced Documents (def:leaf) >
```

```
</MetaDataVersion>
</Study>
</ODM>
```

# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study



## Define-XML 2.0 Key Metadata Components



# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study



## STUDY LEVEL METADATA

Study Level Metadata (SLM) UI is used to switch the Define-XML 1.0 to Define-XML 2.0. The system automatically initiates the change in metadata information for the specific study once the user switches to a different define version at the time of saving the UI. In addition to change, user needs to configure additional information such as value list, comments for the target define version which may not be available in the previous version

The SLM UI capture the below details,

- ODM Attributes such as stylesheet information, File Type, File OID, Creation Date Time and Originator
- Study Global Variables
- Metadata Version Details such as Define-XML version, Standard Name, Standard Version
- Annotated Case Report Forms
- Reference Documents such as reviewer's guide, computational algorithms etc.,
- Display order and names of the Classes

# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study

## DOMAIN LEVEL METADATA



CDISC SDTM study domains are modeled as tables where the columns represent variables and the rows represent observed or derived values of those variables. Domain level metadata is represented in Define-XML as an **ItemGroupDef** element for both version 1 and 2. The system permits the user to view with additional information pertaining to domain level changes using the DLM UI.

| Datasets for Study PhUSE2016-Define-XMLV1 |                                                         |                 |                                                                                                     |            |                                                            |                            |  |
|-------------------------------------------|---------------------------------------------------------|-----------------|-----------------------------------------------------------------------------------------------------|------------|------------------------------------------------------------|----------------------------|--|
| Dataset                                   | Description                                             | Class           | Structure                                                                                           | Purpose    | Keys                                                       | Location                   |  |
| TA                                        | <a href="#">Trial Arms</a>                              | TRIAL DESIGNS   | One record per planned Element per Arm                                                              | Tabulation | STUDYID, ARMCD, TAETORD                                    | <a href="#">ta.xpt</a>     |  |
| TD                                        | <a href="#">Trial Disease Assessment</a>                | TRIAL DESIGNS   | One record per planned constant assessment period                                                   | Tabulation | STUDYID, TDORDER, TDANCVAR, TDSTOFF, TDTGTPAI              | <a href="#">td.xpt</a>     |  |
| TE                                        | <a href="#">Trial Elements</a>                          | TRIAL DESIGNS   | One record per planned Element                                                                      | Tabulation | STUDYID, ETCD                                              | <a href="#">te.xpt</a>     |  |
| TI                                        | <a href="#">Trial Inclusion/Exclusion Criteria</a>      | TRIAL DESIGNS   | One record per I/E criterion                                                                        | Tabulation | STUDYID, IETESTCD                                          | <a href="#">ti.xpt</a>     |  |
| TS                                        | <a href="#">Trial Summary</a>                           | TRIAL DESIGNS   | One record per trial summary parameter value                                                        | Tabulation | STUDYID, TSPARMCD, TSSEQ                                   | <a href="#">ts.xpt</a>     |  |
| TV                                        | <a href="#">Trial Visits</a>                            | TRIAL DESIGNS   | One record per planned Visit per Arm                                                                | Tabulation | STUDYID, VISITNUM, ARMCD                                   | <a href="#">tv.xpt</a>     |  |
| CO                                        | <a href="#">Comments</a>                                | SPECIAL-PURPOSE | One record per comment per subject                                                                  | Tabulation | STUDYID, USUBJID, RDOMAIN, IDVAR, IDVARVAL                 | <a href="#">co.xpt</a>     |  |
| DM                                        | <a href="#">Demographics</a>                            | SPECIAL-PURPOSE | One record per subject                                                                              | Tabulation | STUDYID, USUBJID                                           | <a href="#">dm.xpt</a>     |  |
| SE                                        | <a href="#">Subject Elements</a>                        | SPECIAL-PURPOSE | One record per actual Element per subject                                                           | Tabulation | STUDYID, USUBJID, TAETORD                                  | <a href="#">se.xpt</a>     |  |
| SV                                        | <a href="#">Subject Visits</a>                          | SPECIAL-PURPOSE | One record per actual visit per subject                                                             | Tabulation | STUDYID, USUBJID, VISITNUM                                 | <a href="#">sv.xpt</a>     |  |
| CM                                        | <a href="#">Concomitant Medications</a>                 | INTERVENTIONS   | One record per recorded medication occurrence or constant-dosing interval per subject               | Tabulation | STUDYID, USUBJID, CMTRT, CMDOSE, CMCAT, CMSTDTCD, CMDOSFRQ | <a href="#">cm.xpt</a>     |  |
| EX                                        | <a href="#">Exposure</a>                                | INTERVENTIONS   | One record per constant dosing interval per subject                                                 | Tabulation | STUDYID, USUBJID, EXTRT, EXSTDTC                           | <a href="#">ex.xpt</a>     |  |
| AE                                        | <a href="#">Adverse Events</a>                          | EVENTS          | One record per adverse event per subject                                                            | Tabulation | STUDYID, USUBJID, AEDECOD, AESTDTC                         | <a href="#">ae.xpt</a>     |  |
| DS                                        | <a href="#">Disposition</a>                             | EVENTS          | One record per disposition status or protocol milestone per subject                                 | Tabulation | STUDYID, USUBJID, DSDECOD, DSSTDTC                         | <a href="#">ds.xpt</a>     |  |
| MH                                        | <a href="#">Medical History</a>                         | EVENTS          | One record per medical history event per subject                                                    | Tabulation | STUDYID, USUBJID, MHTERM, MHSTDTC                          | <a href="#">mh.xpt</a>     |  |
| EG                                        | <a href="#">ECG Test Results</a>                        | FINDINGS        | One record per ECG observation per visit per subject                                                | Tabulation | STUDYID, USUBJID, EGDTC, EGECAT, EGTESTCD                  | <a href="#">eg.xpt</a>     |  |
| LB01                                      | <a href="#">Laboratory Tests Results Hematology</a>     | FINDINGS        | One record per analyte per visit per subject                                                        | Tabulation | STUDYID, USUBJID, LBDTC, LBCAT, LBSCAT, LBTESTCD           | <a href="#">lb01.xpt</a>   |  |
| LB02                                      | <a href="#">Laboratory Tests Results non Hematology</a> | FINDINGS        | One record per analyte per visit per subject                                                        | Tabulation | STUDYID, USUBJID, LBDTC, LBCAT, LBSCAT, LBTESTCD           | <a href="#">lb02.xpt</a>   |  |
| NS                                        | <a href="#">Custom Domain (NS)</a>                      | FINDINGS        | One record per analyte per planned time point number per time point reference per visit per subject | Tabulation | STUDYID, USUBJID, NSDTC, NSCAT, NSSCAT, NSTESTCD           | <a href="#">ns.xpt</a>     |  |
| QS                                        | <a href="#">Questionnaires</a>                          | FINDINGS        | One record per questionnaire per question per time point per visit per subject                      | Tabulation | STUDYID, USUBJID, QSDTC, VISITNUM, QSCAT, QSSCAT, QSTESTCD | <a href="#">qs.xpt</a>     |  |
| VS                                        | <a href="#">Vital Signs</a>                             | FINDINGS        | One record per vital sign measurement per visit per subject                                         | Tabulation | STUDYID, USUBJID, VSDTC, VISITNUM, VSCAT, VSTESTCD         | <a href="#">vs.xpt</a>     |  |
| FA                                        | <a href="#">Findings About Events or Interventions</a>  | FINDINGS        | One record per finding per object per time point per time point reference per visit per subject     | Tabulation | STUDYID, USUBJID, FACAT, FASPID, FAOBJ, FADTC              | <a href="#">fa.xpt</a>     |  |
| RELREC                                    | <a href="#">Related Records</a>                         | RELATIONSHIP    | One record per related record, group of records or dataset                                          | Tabulation | STUDYID, USUBJID, RELID, RDOMAIN, IDVAR, IDVARVAL          | <a href="#">relrec.xpt</a> |  |
| SUPDDM                                    | <a href="#">Supplemental Qualifiers for DM</a>          | RELATIONSHIP    | One record per IDVAR, IDVARVAL, and ONAM value per subject                                          | Tabulation | STUDYID, USUBJID, RDOMAIN, IDVAR, IDVARVAL, ONAM           | <a href="#">supddm.xpt</a> |  |

# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study

## DOMAIN LEVEL METADATA



CDISC SDTM study domains are modeled as tables where the columns represent variables and the rows represent observed or derived values of those variables. Domain level metadata is represented in Define-XML as an **ItemGroupDef** element for both version 1 and 2. The system permits the user to view with additional information pertaining to domain level changes using the DLM UI.

SDTM-IG 3.2

+ Annotated Case Report Form

+ Reviewers Guide

+ Complex Algorithms

+ Tabulation Datasets

- Trial Arms (TA)

- Trial Elements (TE)

- Trial Inclusion/Exclusion Criteria (TI)

- Trial Summary (TS)

- Trial Visits (TV)

- Comments (CO)

- Demographics (DM)

- Subject Elements (SE)

- Subject Visits (SV)

- Concomitant Medications (CM)

- Exposure (EX)

- Adverse Events (AE)

- Disposition (DS)

- Medical History (MH)

Datasets for Study PhUSE2016-Define-XMLV1

| Dataset | Description                                        | Class         | Structure                                         | Purpose    | Keys                                          | Location               |
|---------|----------------------------------------------------|---------------|---------------------------------------------------|------------|-----------------------------------------------|------------------------|
| TA      | <a href="#">Trial Arms</a>                         | TRIAL DESIGNS | One record per planned Element per Arm            | Tabulation | STUDYID, ARMCD, TAETORD                       | <a href="#">ta.xpt</a> |
| TD      | <a href="#">Trial Disease Assessment</a>           | TRIAL DESIGNS | One record per planned constant assessment period | Tabulation | STUDYID, TDORDER, TDANCVAR, TDSTOFF, TDTGTPAI | <a href="#">td.xpt</a> |
| TE      | <a href="#">Trial Elements</a>                     | TRIAL DESIGNS | One record per planned Element                    | Tabulation | STUDYID, ETCDD                                | <a href="#">te.xpt</a> |
| TI      | <a href="#">Trial Inclusion/Exclusion Criteria</a> | TRIAL DESIGNS | One record per I/E criterion                      | Tabulation | STUDYID, IETESTCD                             | <a href="#">ti.xpt</a> |
| TS      | <a href="#">Trial Summary</a>                      | TRIAL DESIGNS | One record per trial summary parameter value      | Tabulation | STUDYID, TSPARMCD, TSSEQ                      | <a href="#">ts.xpt</a> |

| Dataset | Description                                        | Class           | Structure                                    | Purpose    | Keys                                       | Location                 | Documentation                                                                                                                                            |
|---------|----------------------------------------------------|-----------------|----------------------------------------------|------------|--------------------------------------------|--------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| TA      | <a href="#">Trial Arms</a>                         | TRIAL DESIGN    | One record per planned Element per Arm       | Tabulation | STUDYID, ARMCD, TAETORD                    | <a href="#">ta.xpt</a>   |                                                                                                                                                          |
| TE      | <a href="#">Trial Elements</a>                     | TRIAL DESIGN    | One record per planned Element               | Tabulation | STUDYID, ETCDD                             | <a href="#">te.xpt</a>   |                                                                                                                                                          |
| TI      | <a href="#">Trial Inclusion/Exclusion Criteria</a> | TRIAL DESIGN    | One record per I/E criterion                 | Tabulation | STUDYID, IETESTCD                          | <a href="#">ti.xpt</a>   |                                                                                                                                                          |
| TS      | <a href="#">Trial Summary</a>                      | TRIAL DESIGN    | One record per trial summary parameter value | Tabulation | STUDYID, TSPARMCD, TSSEQ                   | <a href="#">ts.xpt</a>   |                                                                                                                                                          |
| TV      | <a href="#">Trial Visits</a>                       | TRIAL DESIGN    | One record per planned Visit per Arm         | Tabulation | STUDYID, VISITNUM, ARMCD                   | <a href="#">tv.xpt</a>   |                                                                                                                                                          |
| CO      | <a href="#">Comments</a>                           | SPECIAL PURPOSE | One record per comment per subject           | Tabulation | STUDYID, USUBJID, RDOMAIN, IDVAR, IDVARVAL | <a href="#">co.xpt</a>   |                                                                                                                                                          |
| DM      | <a href="#">Demographics</a>                       | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, USUBJID                           | <a href="#">dm.xpt</a>   | See Reviewer's Guide, Section 2.1 Demographics<br><a href="#">Reviewers Guide</a>                                                                        |
| SE      | <a href="#">Subject Elements</a>                   | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, USUBJID                           | <a href="#">se.xpt</a>   |                                                                                                                                                          |
| SV      | <a href="#">Subject Visits</a>                     | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, USUBJID                           | <a href="#">sv.xpt</a>   |                                                                                                                                                          |
| CM      | <a href="#">Concomitant Medications</a>            | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, CMTRT, LCAT, CMSTDTC              | <a href="#">cm.xpt</a>   |                                                                                                                                                          |
| EX      | <a href="#">Exposure</a>                           | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, EXTRT                             | <a href="#">ex.xpt</a>   |                                                                                                                                                          |
| AE      | <a href="#">Adverse Events</a>                     | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, AESTDTC                           | <a href="#">ae.xpt</a>   |                                                                                                                                                          |
| DS      | <a href="#">Disposition</a>                        | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, DSSTDTC                           | <a href="#">ds.xpt</a>   |                                                                                                                                                          |
| MH      | <a href="#">Medical History</a>                    | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, HSTDTC                            | <a href="#">mh.xpt</a>   |                                                                                                                                                          |
| EG      | <a href="#">Exposure</a>                           | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, EGDTCT, ESTCD                     | <a href="#">eg.xpt</a>   |                                                                                                                                                          |
| LB      | <a href="#">Laboratory Data</a>                    | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, LBOTCT, LCAT, LBTESTCD            | <a href="#">lb01.xpt</a> | LB is submitted as a split dataset. The split was done based on LBCAT. When LBCAT=HEMATOLOGY then data is saved in LB01. All other data is saved in LB02 |
| LB      | <a href="#">Laboratory Data</a>                    | SPECIAL PURPOSE | One record per subject                       | Tabulation | STUDYID, LBOTCT, LCAT, LBTESTCD            | <a href="#">lb02.xpt</a> | LB is submitted as a split dataset. The split was done based on LBCAT. When LBCAT=HEMATOLOGY then data is saved in LB01. All other data is saved in LB02 |

Class Name Special-Purpose Domains

Domain Name DM

Structure One record per subject

User Notes

☐ Is Repeat Data

☐ Is Reference Data

Key Variables STUDYID, USUBJID

--SEQ Generation Based On USUBJID

Brief Notes Demographics includes a set of essential standard variables that describe each subject in a clinical study. It is the parent domain for all other observations for human clinical subjects.

Comment OID DOMAIN.DM

Comment OID DOMAIN.DM

Description See Reviewer's Guide, Section 2.1 Demographics

Document Details

| Document          | Page Number | Named Description |
|-------------------|-------------|-------------------|
| 1 Reviewers Guide | section2.1  | ✓                 |

Share Browser WebEx

eneration: 2016-03-16T06:55:43

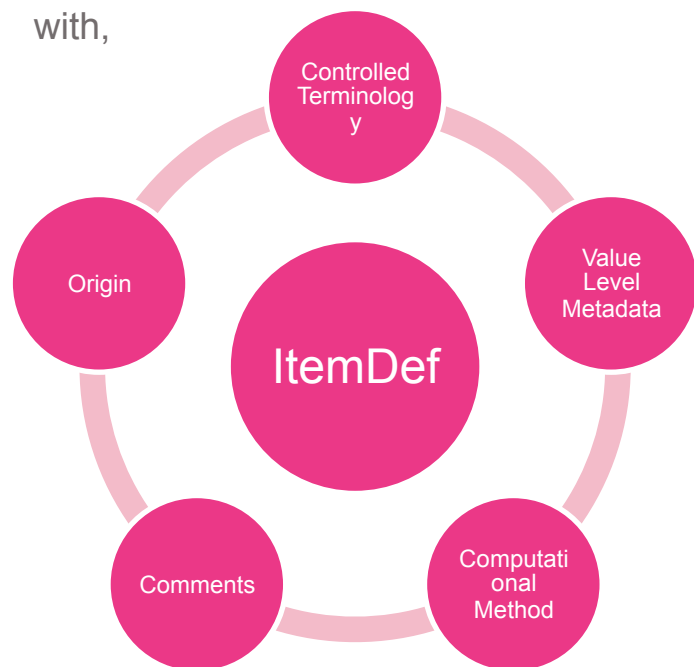
Stylesheet version: 2013-04-24

# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study

## VARIABLE LEVEL METADATA



Define-XML version represents variable metadata using an ItemDef element in both the versions and it's associated with,



The way of representing the XML elements differs on Define-XML version 1 and 2.

### Define-XML V1 (VLM)

| Variable  | Label                              | Type     | Controlled Terms or Format | Origin       | Role               | Comment                                                                                                                                                              |
|-----------|------------------------------------|----------|----------------------------|--------------|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| STUDYID   | Study Identifier                   | text     |                            | Protocol     | IDENTIFIER         |                                                                                                                                                                      |
| DOMAIN    | Domain Abbreviation                | text     |                            | Assigned     | IDENTIFIER         | Two-character abbreviation for the domain most relevant to the observation. The I also used as a prefix for variables to ensure uniqueness when datasets are merged. |
| USUBJID   | Unique Subject Identifier          | text     |                            | Derived      | IDENTIFIER         | See Computational Method: <a href="#">COMPMETHOD USUBJID</a>                                                                                                         |
| SUBJID    | Subject Identifier for the Study   | text     |                            | CRF Page 1   | TOPIC              |                                                                                                                                                                      |
| RFSTDTCT  | Subject Reference Start Date/Time  | datetime | ISO8601                    | Derived      | RECORD QUALIFIER   | See Computational Method: <a href="#">COMPMETHOD RFSTDTCT</a>                                                                                                        |
| RFENDTCT  | Subject Reference End Date/Time    | datetime | ISO8601                    | Derived      | RECORD QUALIFIER   | See Computational Method: <a href="#">COMPMETHOD RFENDTCT</a>                                                                                                        |
| RFNSTDTCT | Date/Time of First Study Treatment | datetime | ISO8601                    | Derived      | RECORD QUALIFIER   | See Computational Method: <a href="#">COMPMETHOD RFNSTDTCT</a>                                                                                                       |
| RFENDTCT  | Date/Time of Last Study Treatment  | datetime | ISO8601                    | Derived      | RECORD QUALIFIER   | See Computational Method: <a href="#">COMPMETHOD RFENDTCT</a>                                                                                                        |
| RFICDTC   | Date/Time of Informed Consent      | date     | ISO8601                    | CRF Page 1   | RECORD QUALIFIER   |                                                                                                                                                                      |
| RFENDTCT  | Date/Time of End of Participation  | date     | ISO8601                    | Derived      | RECORD QUALIFIER   | See Computational Method: <a href="#">COMPMETHOD RFENDTCT</a>                                                                                                        |
| DTHTCT    | Date/Time of Death                 | date     | ISO8601                    | CRF Page 907 | RECORD QUALIFIER   | From AE page; when outcome is Death then Y then date/time, else Null                                                                                                 |
| DTHTFL    | Subject Death Flag                 | text     | YES                        | CRF Page 907 | RECORD QUALIFIER   | From AE page; when outcome is Death then Y, else Null                                                                                                                |
| SITEID    | Study Site Identifier              | text     |                            | Assigned     | RECORD QUALIFIER   |                                                                                                                                                                      |
| BRTHDTC   | Date/Time of Birth                 | date     | ISO8601                    | CRF Page 1   | RECORD QUALIFIER   |                                                                                                                                                                      |
| AGE       | Age                                | integer  |                            | Derived      | RECORD QUALIFIER   | See Computational Method: <a href="#">COMPMETHOD AGE</a>                                                                                                             |
| AGEU      | Age Units                          | text     |                            | Assigned     | VARIABLE QUALIFIER | Defaulted to YEARS                                                                                                                                                   |
| SEX       | Sex                                | text     | SEX                        | CRF Page 1   | RECORD QUALIFIER   |                                                                                                                                                                      |
| RACE      | Race                               | text     | RACE                       | CRF Page 1   | RECORD QUALIFIER   |                                                                                                                                                                      |
| ETHNIC    | Ethnicity                          | text     | ETHNIC                     | CRF Page 1   | RECORD QUALIFIER   |                                                                                                                                                                      |

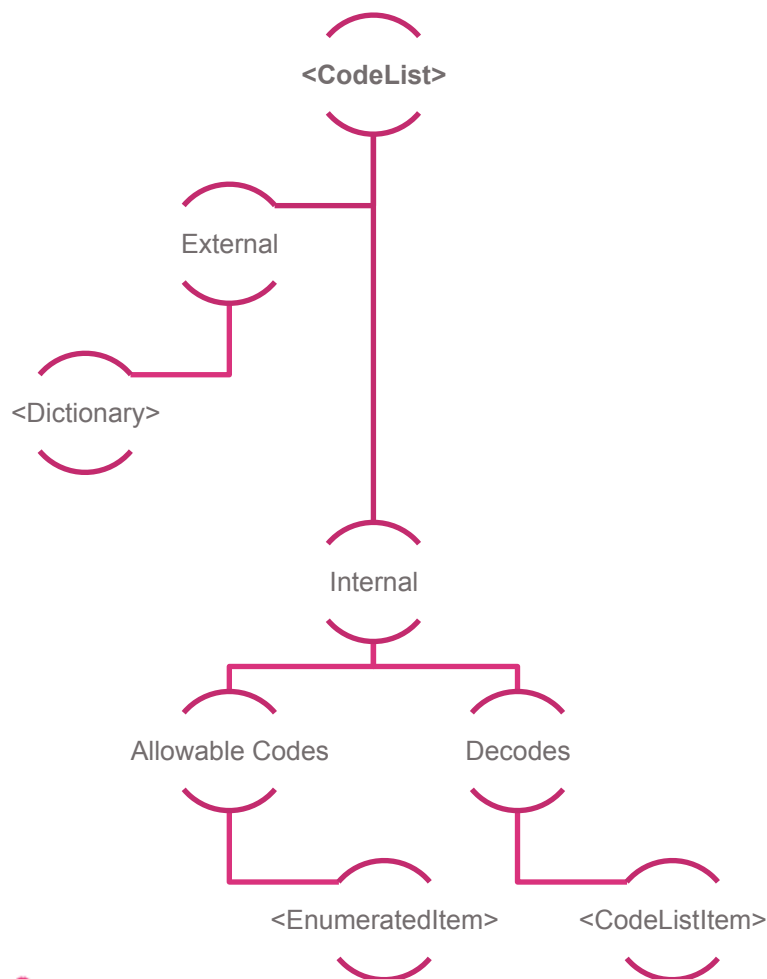
### Define-XML V2 (VLM)

| Variable  | Label                              | Key | Type     | Length | Controlled Terms or Format                    | Origin       | Derivation/Comment                                                                                                                                                                            |
|-----------|------------------------------------|-----|----------|--------|-----------------------------------------------|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| STUDYID   | Study Identifier                   | 1   | text     | 40     |                                               | Protocol     |                                                                                                                                                                                               |
| DOMAIN    | Domain Abbreviation                |     | text     | 2      |                                               | Assigned     | Two-character abbreviation for the domain most relevant to the observation. The I also used as a prefix for variables to ensure uniqueness when datasets are merged.                          |
| USUBJID   | Unique Subject Identifier          | 2   | text     | 20     |                                               | Derived      | Concatenation of STUDYID and SUBJID                                                                                                                                                           |
| SUBJID    | Subject Identifier for the Study   |     | text     | 3      |                                               | CRF Page 1   |                                                                                                                                                                                               |
| RFSTDTCT  | Subject Reference Start Date/Time  |     | datetime |        | ISO8601                                       | Derived      | RFSTDTCT = First date/time of study drug treatment                                                                                                                                            |
| RFENDTCT  | Subject Reference End Date/Time    |     | datetime |        | ISO8601                                       | Derived      | RFENDTCT = Date of Completion or date of Withdrawal. Null for screen                                                                                                                          |
| RFNSTDTCT | Date/Time of First Study Treatment |     | datetime |        | ISO8601                                       | Derived      | RFNSTDTCT = Date/time of first exposure to protocol specified treatment                                                                                                                       |
| RFENDTCT  | Date/Time of Last Study Treatment  |     | datetime |        | ISO8601                                       | Derived      | RFENDTCT = Date/time of last exposure to protocol specified treatment                                                                                                                         |
| RFICDTC   | Date/Time of Informed Consent      |     | date     |        | ISO8601                                       | CRF Page 1   |                                                                                                                                                                                               |
| RFENDTCT  | Date/Time of End of Participation  |     | date     |        | ISO8601                                       | Derived      | RFENDTCT = Date/time when subject ended participant or follow-up                                                                                                                              |
| DTHTCT    | Date/Time of Death                 |     | date     |        | ISO8601                                       | CRF Page 907 | From AE page; when outcome is Death then Y then date/time, else Null                                                                                                                          |
| DTHTFL    | Subject Death Flag                 |     | text     | 1      | ["Y" = "Yes"]<br><No Yes Response Subset (Y)> | CRF Page 907 | From AE page; when outcome is Death then Y, else Null                                                                                                                                         |
| SITEID    | Study Site Identifier              |     | text     | 3      |                                               | Assigned     |                                                                                                                                                                                               |
| BRTHDTC   | Date/Time of Birth                 |     | date     |        | ISO8601                                       | CRF Page 1   |                                                                                                                                                                                               |
| AGE       | Age                                |     | integer  | 8      |                                               | Derived      | Age at Screening Date (Screening Date - Birth date). For the complete document, Reviewers Guide ( <a href="#">reviewersguide.pdf</a> ) Reviewers Guide ( <a href="#">reviewersguide.pdf</a> ) |
| AGEU      | Age Units                          |     | text     | 5      |                                               | Assigned     | Defaulted to YEARS                                                                                                                                                                            |
| SEX       | Sex                                |     | text     | 1      | ["F" = "Female", "M" = "Male"]<br><Sex>       | CRF Page 1   |                                                                                                                                                                                               |
| RACE      | Race                               |     | text     | 8      | Race                                          | CRF Page 1   |                                                                                                                                                                                               |
| ETHNIC    | Ethnicity                          |     | text     | 22     | ["HISPANIC OR LATINO", "NOT                   | CRF Page 1   |                                                                                                                                                                                               |

# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study

## CODE LISTS

The term "Controlled Terminology" in the context of a study refers to the set of all allowable values across all variables that have finite sets of allowable values in the study. A "Codelist" is a unique subset of the controlled terminology to which one or more variables are subject



| Controlled Terminology (CODE LIST) |  |                    |
|------------------------------------|--|--------------------|
|                                    |  | ACN, R             |
| Code Value                         |  | Define-XML V1 (CL) |
| DOSE NOT CHANGED                   |  |                    |
| DRUG WITHDRAWN                     |  | DRUG WITHDRAWN     |
| NOT APPLICABLE                     |  | NOT APPLICABLE     |
| AEENRF, Reference Name (AEENRF)    |  |                    |
| Code Value                         |  | Code Text          |
| AFTER                              |  | AFTER              |
| DURING/AFTER                       |  | DURING/AFTER       |
| AEREL, Reference Name (AEREL)      |  |                    |
| Code Value                         |  | Code Text          |
| DEFINITE                           |  | DEFINITE           |
| POSSIBLY                           |  | POSSIBLY           |
| PROBABLE                           |  | PROBABLE           |
| UNLIKELY                           |  | UNLIKELY           |
| UNRELATED                          |  | UNRELATED          |
| AESEV, Reference Name (AESEV)      |  |                    |
| Code Value                         |  | Code Text          |
| MILD                               |  | MILD               |
| MODERATE                           |  | MODERATE           |
| SEVERE                             |  | SEVERE             |
| ARM, Reference Name (ARM)          |  |                    |
| Code Value                         |  | Code Text          |
| 2 mg Filgrastin                    |  | 2 mg Filgrastin    |
| ARMCD, Reference Name (ARMCD)      |  |                    |
| Code Value                         |  | Code Text          |
| A                                  |  | 2 mg Filgrastin    |

### Relation to Reference Period (AEENRF) [CL.AEENRF, C00720]

| Permitted Value (Code) |
|------------------------|
| AFTER [C38008]         |
| DURING/AFTER [C49640]  |

### Causality [CL.AEREL]

| Permitted Value (Code) |
|------------------------|
| UNRELATED              |
| UNLIKELY               |
| POSSIBLY               |
| PROBABLE               |
| DEFINITE               |

### Define-XML V2 (CL)

### Severity/Intensity Scale for Adverse Events [CL.AESEV, C66769]

| Permitted Value (Code) |
|------------------------|
| MILD [C41338]          |
| MODERATE [C41339]      |
| SEVERE [C41340]        |

### Description of Planned Arm [CL.ARM]

| Permitted Value (Code) |
|------------------------|
| 2 mg Filgrastin        |

### Planned Arm Code [CL.ARMCD]

| Permitted Value (Code) | Display Value (Decode) |
|------------------------|------------------------|
| A                      | 2 mg Filgrastin        |

### Units for Vital Signs Results (CM only) [CL.CM, C66770]

| Permitted Value (Code) | Display Value (Decode) |
|------------------------|------------------------|
| cm [C49668]            | Centimeter             |

# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study



## CODE LISTS

EXACT can import the SDTM Terminology spreadsheet published in CDISC eSHARE downloads (SDTM Terminology Section) and based on the Define-XML version, it populates the C-code information, permitted values etc.,

<http://www.cdisc.org/members-only/eshare-downloads>

<https://www.cancer.gov/research/resources/terminology/cdisc>

| SDTM Terminology |                  |         |          |                                                                                                 |
|------------------|------------------|---------|----------|-------------------------------------------------------------------------------------------------|
| 2016-07-5        | SDTM Terminology | 2016-06 | Metadata | <a href="#">ODM v1.3.1</a>   <a href="#">RDF</a>   <a href="#">Excel</a>   <a href="#">Diff</a> |
| 2016-05-26       | SDTM Terminology | 2016-03 | Metadata | <a href="#">ODM v1.3.1</a>   <a href="#">RDF</a>   <a href="#">Excel</a>   <a href="#">Diff</a> |
| 2016-02-12       | SDTM Terminology | 2015-12 | Metadata | <a href="#">ODM v1.3.1</a>   <a href="#">RDF</a>   <a href="#">Excel</a>   <a href="#">Diff</a> |

| Code   | Codelist Code | Codelist Extensible (Yes/No) | Codelist Name                     | CDISC Submission Value | CDISC Synonym(s)                  | CDISC Definition                                                                                                                  | NCI Preferred Term                                       |
|--------|---------------|------------------------------|-----------------------------------|------------------------|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|
| C66767 |               | No                           | Action Taken with Study Treatment | ACN                    | Action Taken with Study Treatment | Terminology specifying changes to the study treatment as a result of an adverse event.                                            | CDISC SDTM Action Taken with Study Treatment Terminology |
| C49503 | C66767        |                              | Action Taken with Study Treatment | DOSE INCREASED         |                                   | An indication that a medication schedule was modified by addition, either by changing the frequency, strength or amount. (NCI)    | Dose Increased                                           |
| C49504 | C66767        |                              | Action Taken with Study Treatment | DOSE NOT CHANGED       |                                   | An indication that a medication schedule was maintained. (NCI)                                                                    | Dose Not Changed                                         |
| C49505 | C66767        |                              | Action Taken with Study Treatment | DOSE REDUCED           |                                   | An indication that a medication schedule was modified by subtraction, either by changing the frequency, strength or amount. (NCI) | Dose Reduced                                             |
| C49501 | C66767        |                              | Action Taken with Study Treatment | DRUG INTERRUPTED       |                                   | An indication that a medication schedule was modified by temporarily terminating a prescribed regimen of medication. (NCI)        | Drug Interrupted                                         |
| C49502 | C66767        |                              | Action Taken with Study Treatment | DRUG WITHDRAWN         |                                   | An indication that a medication schedule was modified through termination of a prescribed regimen of medication. (NCI)            | Drug Withdrawn                                           |
| C48660 | C66767        |                              | Action Taken with Study Treatment | NOT APPLICABLE         | NA: Not Applicable                | Determination of a value is not relevant in the current context. (NCI)                                                            | Not Applicable                                           |
| C17998 | C66767        |                              | Action Taken with Study Treatment | UNKNOWN                | U: Unknown                        | Not known, not observed, not recorded, or refused. (NCI)                                                                          | Unknown                                                  |

**View Code List**

Code:  CT Name:

Code List Name:

SAS Format Name:

Code List Type:

ODM Data Type:

Code List Label:

CDISC Preferred Term:

CDISC Synonym(s):

CDISC Definition:

☐ Is Extensible ☐ Include Order Number in Define

| Order | Code   | Code List Value  | Code List Text   | CDISC Submission Value | CDISC Preferred Term | CDISC Synonym(s)   |
|-------|--------|------------------|------------------|------------------------|----------------------|--------------------|
| 1     | C49503 | DOSE INCREASED   | DOSE INCREASED   | DOSE INCREASED         |                      |                    |
| 2     | C49504 | DOSE NOT CHANGED | DOSE NOT CHANGED | DOSE NOT CHANGED       |                      |                    |
| 3     | C49505 | DOSE REDUCED     | DOSE REDUCED     | DOSE REDUCED           |                      |                    |
| 4     | C49501 | DRUG INTERRUPTED | DRUG INTERRUPTED | DRUG INTERRUPTED       |                      |                    |
| 5     | C49502 | DRUG WITHDRAWN   | DRUG WITHDRAWN   | DRUG WITHDRAWN         |                      |                    |
| 6     | C48660 | NOT APPLICABLE   | NOT APPLICABLE   | NOT APPLICABLE         |                      | NA: Not Applicable |
| 7     | C17998 | UNKNOWN          | UNKNOWN          | UNKNOWN                |                      | U: Unknown         |

Cancel

Download from  
CDISC eSHARE  
or NCI

Import into  
EXACT

Auto-attached to  
SDTM Variable

Define-XML

# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study

## VALUE LEVEL METADATA

Value Level Metadata

Where Clause Name: LBORRES.BASO Where Clause Comment OID: Select

| Domain | Variable | Comparator | Check Value | Soft/Hard |
|--------|----------|------------|-------------|-----------|
| LB     | LBTESTCD | EQ         | BASO        | Soft      |
| LB     | LBCAT    | EQ         | HEMATOLOGY  | Soft      |

Metadata Details

Name: LBTESTCD

Label: Basophils

Order Number: 22 Mandatory: No

Role: Select

Type: float

Length: 8

Significant Digits: 2

Display Format:

Origin:  
☐ Derived  
☐ CRF Page  
☒ eDT  
☐ Assigned  
☐ Protocol

SAS Field Name:

Computation OID: Select

Code List / Control Terminology

☒ Code List: Select Code List Name:

☐ List of Controlled Terms (e.g., YEARS, MONTHS, DAYS)

Comment (define.xml):

Comment OID: Select

Close

In EXACT, the Value Level Metadata can be configured either through user interface or an excel spreadsheet using the import functionality

# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study

## VALUE LEVEL METADATA

--ORRES

--TESTCD <conditional operator> "value"

--TESTCD <conditional operator> "value" <conditional operator> "Value"

--TESTCD <conditional operator> "value" <IN/NOTIN> ("Value1", "Value2")

Conditional Operators (Comparator)  
LT, LE, GT, GE, EQ, NE, IN, NOTIN



| Value Level Metadata (ValueList.EG.EGCAT)                        |               |                                        |         |
|------------------------------------------------------------------|---------------|----------------------------------------|---------|
| Source Variable                                                  | Value         | Define-XML V1 (VL)                     | Type    |
| EGCAT                                                            | <no category> |                                        | text    |
| EGCAT                                                            | FINDING       | FINDING                                | text    |
| EGCAT                                                            | INTERVAL      | INTERVAL                               | text    |
| EGCAT                                                            | MEASUREMENT   | MEASUREMENT                            | text    |
| Value Level Metadata (ValueList.EG.EGCAT.<no category>.EGTESTCD) |               |                                        |         |
| Source Variable                                                  | Value         | Label                                  | Type    |
| EGTESTCD                                                         | INTP          | Interpretation                         | text    |
| Value Level Metadata (ValueList.EG.EGCAT.FINDING.EGTESTCD)       |               |                                        |         |
| Source Variable                                                  | Value         | Label                                  | Type    |
| EGTESTCD                                                         | EGABN1        | ECG Abnormality 1                      | text    |
| EGTESTCD                                                         | EGABN2        | ECG Abnormality 2                      | text    |
| Value Level Metadata (ValueList.EG.EGCAT.INTERVAL.EGTESTCD)      |               |                                        |         |
| Source Variable                                                  | Value         | Label                                  | Type    |
| EGTESTCD                                                         | PRMEAN        | Summary (Mean) PR Duration             | integer |
| EGTESTCD                                                         | QRS DUR       | Summary (Mean) QRS Duration            | integer |
| EGTESTCD                                                         | QTcF          | QTcF - Fridericia's Correction Formula | integer |
| EGTESTCD                                                         | QTMEAN        | Summary (Mean) QT Duration             | integer |
| Value Level Metadata (ValueList.EG.EGCAT.MEASUREMENT.EGTESTCD)   |               |                                        |         |
| Source Variable                                                  | Value         | Label                                  | Type    |
| EGTESTCD                                                         | HRMEAN        | Summary (Mean) Heart Rate              | integer |

### Value Level Metadata - EG [EGORRES]

| Variable | Where                                                                                                              | Define-XML V2 (VL) |   |                                                      | or |
|----------|--------------------------------------------------------------------------------------------------------------------|--------------------|---|------------------------------------------------------|----|
|          |                                                                                                                    | Format             |   |                                                      |    |
| EGORRES  | <a href="#">EGTESTCD</a> EQ INTP (Interpretation)                                                                  | text               | 8 | ["ABNORMAL", "NORMAL"]<br><Normal Abnormal Response> |    |
| EGORRES  | <a href="#">EGTESTCD</a> EQ HRMEAN (Summary (Mean) Heart Rate)<br>AND <a href="#">EGCAT</a> EQ MEASUREMENT         | integer            | 2 |                                                      |    |
| EGORRES  | <a href="#">EGTESTCD</a> EQ PRMEAN (Summary (Mean) PR Duration)<br>AND <a href="#">EGCAT</a> EQ INTERVAL           | integer            | 3 |                                                      |    |
| EGORRES  | <a href="#">EGTESTCD</a> EQ QRS DUR (Summary (Mean) QRS Duration)<br>AND <a href="#">EGCAT</a> EQ INTERVAL         | integer            | 3 | ISO8601                                              |    |
| EGORRES  | <a href="#">EGTESTCD</a> EQ QTcF (QTcF - Fridericia's Correction Formula)<br>AND <a href="#">EGCAT</a> EQ INTERVAL | integer            | 3 |                                                      |    |
| EGORRES  | <a href="#">EGTESTCD</a> EQ QTMEAN (Summary (Mean) QT Duration)<br>AND <a href="#">EGCAT</a> EQ INTERVAL           | integer            | 3 |                                                      |    |

|                                                   |                                                                                                                                                                                                                                                                                                            |
|---------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Computational Algorithms (COMPMETHOD.AE.AEENRF)   |                                                                                                                                                                                                                                                                                                            |
| Reference Name                                    | Computation Method                                                                                                                                                                                                                                                                                         |
| COMPMETHOD.AE.AEENRF                              | IF AE is Ongoing and AEENDTC is missing then AEENRF = 'AFTER'; IF AEENDTC is present then AEENRF = 'BEFORE' or 'DURING'.                                                                                                                                                                                   |
| Computational Algorithms (COMPMETHOD.AGE)         |                                                                                                                                                                                                                                                                                                            |
| Reference Name                                    | Computation Method                                                                                                                                                                                                                                                                                         |
| COMPMETHOD.AGE                                    | Age at Screening Date (Screening Date - Birth date). For the complete algorithm see the referenced external document.                                                                                                                                                                                      |
| Computational Algorithms (COMPMETHOD.CLSIG)       |                                                                                                                                                                                                                                                                                                            |
| Reference Name                                    | Computation Method                                                                                                                                                                                                                                                                                         |
| COMPMETHOD.CLSIG                                  | Calculated based on High and Low reference ranges                                                                                                                                                                                                                                                          |
| Computational Algorithms (COMPMETHOD.CM.CMENRF)   |                                                                                                                                                                                                                                                                                                            |
| Reference Name                                    | Computation Method                                                                                                                                                                                                                                                                                         |
| COMPMETHOD.CM.CMENRF                              | IF CM is Ongoing and CMENDTC is missing then CMENRF = 'AFTER'; IF CMENDTC precedes RFSTDTC then CMENRF = 'BEFORE'; IF CMENDTC is on or after RFSTDTC and CMENDTC is on or after RFSTDTC then CMENRF = 'DURING'; IF CMENDTC is partial and coincides with RFENDTC is unclear then CMENRF = 'DURING'/'AFTER' |
| Computational Algorithms (COMPMETHOD.CM.CMSTRF)   |                                                                                                                                                                                                                                                                                                            |
| Reference Name                                    | Computation Method                                                                                                                                                                                                                                                                                         |
| COMPMETHOD.CM.CMSTRF                              | IF CMSTDTC precedes RFSTDTC then CMSTRF = 'BEFORE'; IF CMSTDTC is on or after RFSTDTC and CMSTDTC is on or before RFENDTC then CMSTRF = 'DURING'                                                                                                                                                           |
| Computational Algorithms (COMPMETHOD.DRFL)        |                                                                                                                                                                                                                                                                                                            |
| Reference Name                                    | Computation Method                                                                                                                                                                                                                                                                                         |
| COMPMETHOD.DRFL                                   | The derived flag is Y when the result has been calculated                                                                                                                                                                                                                                                  |
| Computational Algorithms (COMPMETHOD.DY)          |                                                                                                                                                                                                                                                                                                            |
| Reference Name                                    | Computation Method                                                                                                                                                                                                                                                                                         |
| COMPMETHOD.DY                                     | -DY = (date portion of -DTC) - (date portion of RFSTDTC) + 1 if -DTC is on or after RFSTDTC -DY = (date portion of -DTC) - (date portion of RFSTDTC) if -DTC precedes RFSTDTC                                                                                                                              |
| Computational Algorithms (COMPMETHOD.EG.EGSTRESU) |                                                                                                                                                                                                                                                                                                            |
| Reference Name                                    | Computation Method                                                                                                                                                                                                                                                                                         |
| COMPMETHOD.EG.EGSTRESU                            | Is derived from EGORRESU                                                                                                                                                                                                                                                                                   |
| Computational Algorithms (COMPMETHOD.EGBLFL)      |                                                                                                                                                                                                                                                                                                            |
| Reference Name                                    | Computation Method                                                                                                                                                                                                                                                                                         |
| COMPMETHOD.EGBLFL                                 | Safety subjects only: EGBLFL = 'Y' for last record with non Null EGORRES on or before the first dose date (RFSTDTC). Null otherwise                                                                                                                                                                        |
| Computational Algorithms (COMPMETHOD.EDGRVFL)     |                                                                                                                                                                                                                                                                                                            |
| Reference Name                                    | Computation Method                                                                                                                                                                                                                                                                                         |
| COMPMETHOD.EDGRVFL                                | EDGRVFL = 'Y' when EGTSTCD is derived. Null otherwise.                                                                                                                                                                                                                                                     |

| Method                           | Type        | Description                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                  |
|----------------------------------|-------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
| Algorithm to derive AE.AENRNF    | Computation | If AE is Ongoing and AENRNTC is missing then AENRNF = 'AFTER' whether AE ends before or after DM.RFENDTC                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | filled in when J |
| Algorithm to derive AGE          | Computation | Age at Screening Date (Screening Date - Birth date). For the complete algorithm see the referenced external document.<br>Reviewers Guide ( <a href="#">reviewersguide.pdf</a> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                  |
| Algorithm to derive CLSIG        | Computation | Calculated based on High and Low reference ranges<br>Reviewers Guide ( <a href="#">reviewersguide.pdf</a> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                  |
| Algorithm to derive CMENRF       | Computation | If CM is Ongoing and CMENDTC is missing then CMENRF = 'AFTER'; If CMENDTC precedes RFSTDTCT then CMENRF = 'BEFORE'; If CMENDTC is on or after RFENDTC then CMENRF = 'DURING'; If CMENDTC is partial and coincidence with RFENDTC is unclear then CMENRF = 'DURING/AFTER'                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                  |
| Algorithm to derive CMSTRF       | Computation | If CMSTDTCT precedes RFSTDTCT then CMSTRF = 'BEFORE'; If CMSTDTCT is on or after RFSTDTCT and CMSTDTCT is on or before RFENDTC then CMSTRF = '1'                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                  |
| Algorithm to derive Derived Flag | Computation | The derived flag is Y when the result has been calculated                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                  |
| Algorithm to derive xxDY         | Computation | --DY = (date portion of --DTC) - (date portion of RFSTDTCT) + 1 if --DTC is on or after RFSTDTCT --DY = (date portion of --DTC) - (date portion of RFSTDTCT)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |
| Algorithm to derive EG unit      | Computation | Is derived from EGORRESU                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                  |
| Algorithm to derive EGBLFL       | Computation | Safety subjects only: EGBLFL = 'Y' for last record with non Null EGORRES on or before the first dose date (RFSTDTCT). Null otherwise<br>proc sql; create table e /* " all records from EX and LB combined */<br>using l.usubjld e.usubjld /* SUBJID should be the same for LB and EX */ and (scan(l.visit,3) /* =scan(e.visit,3) /* = "P1" or l.visit="UNSCHEDULED" */ period Px should be the same for LB and EX. SCORE belongs to P1 /* " always include all UNSCHEDULEDS" when before dosing */ group by l.usubjld, l.teststdt, l.eppos, e.periodx /* keep a record per SUBJID,TEST, POS and dosing period */ having (l.edgtc=max(l.edgtc) /* and e.edgtc=min(e.edgtc) /* for UNSCHED, keep the lowest EXSTDTCT /* order by l.studyid, l.usubjld, l.edgtc, l.eppos, l.teststdt, l.eppos eg_bln (ln=b KEEP=studyid usubjld edgtc eppos egpos); by l.studyid usubjld edgtc eppos epposstdt egpos; if b then egblfl="Y"; /* when in cc, eg = "EGBLN" then egblfl="--"; /* assign no baseline flag to abnormalities */ run; |                  |
| Algorithm to derive EGRDVL       | Computation | EGDRVFL = 'Y' when EGTESTCD is derived. Null otherwise.<br>Complex Algorithms ( <a href="#">complexalgorithms.pdf</a> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                  |
| Algorithm to derive EGSTRES      | Computation | Data collected in non-standard units is converted using standard conversion factors to standard units.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                  |
| Algorithm to derive EGSTRESN     | Computation | EGSTRESN = numeric value of EGSTRES, when EGSTRES contains numeric data.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                  |
| Algorithm to derive xxENDY       | Computation | --ENDY = (date portion of --ENDTC) - (date portion of RFSTDTCT) + 1 if --ENDTC is on or after RFSTDTCT --ENDY = (date portion of --ENDTC) - (date portion of RFSTDTCT)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                  |

## Description

## Document Reference

## Formal Expression

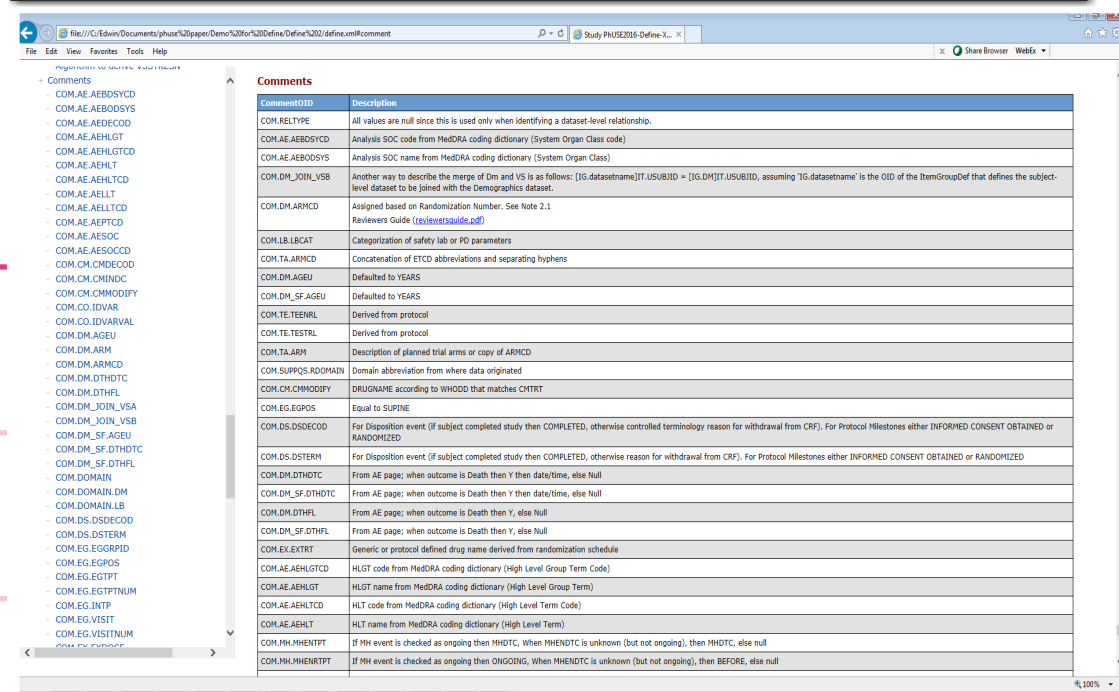
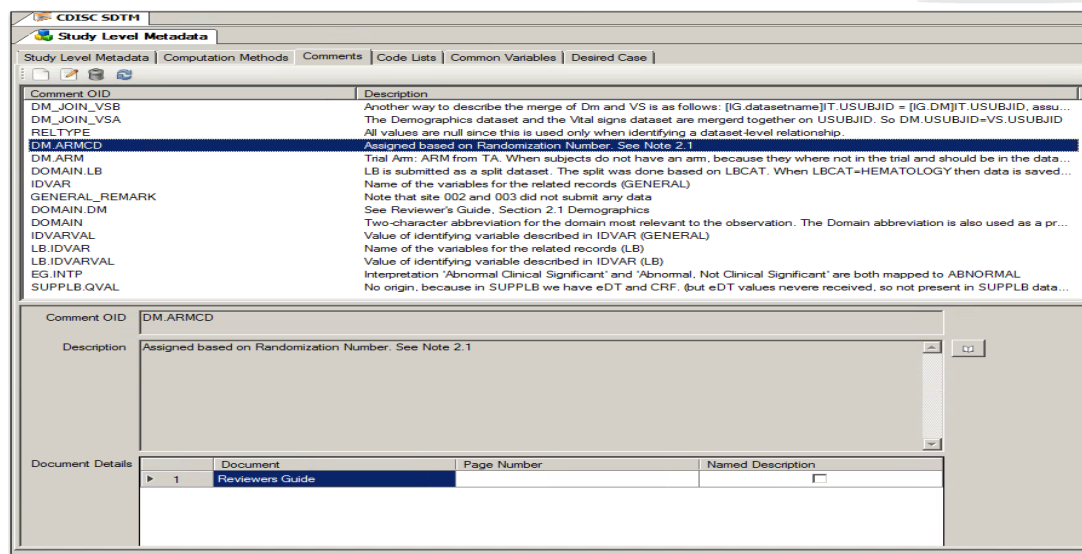


# Handling Define-XML Version 1.0 to Define-XML Version 2.0 in a Study COMMENTS



Define-XML v2.0 allows the definition of comments at dataset, variable and value levels. The mechanism allows referencing short comments self-contained in the Define-XML document or long comments referenced in external documents. For comments in external documents, the reference can include specific pages within the document. Comments are not intended to replace a properly defined computational algorithm, which is expected for derived variables. Define-XML version 1 had very limited possibilities for providing comments related to the various metadata objects in a clinical study.

For Define-XML the comments are displayed along with the variable and value definitions



Comments

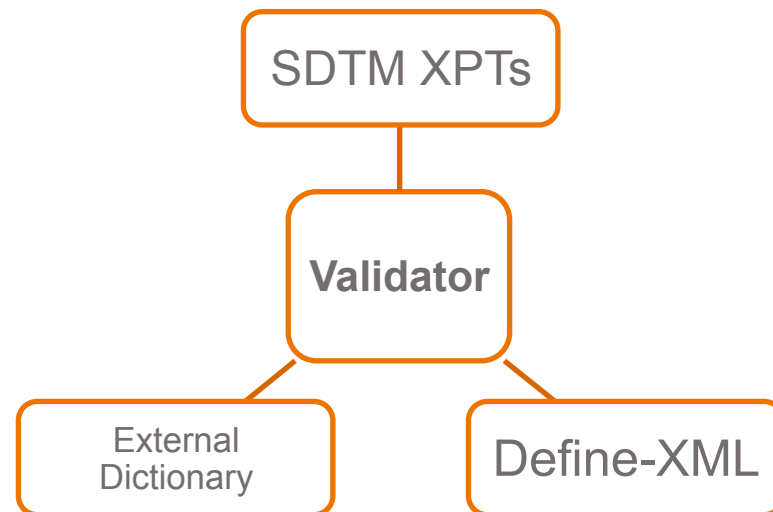
Description

Document Reference



PRAHEALTHSCIENCES

**PINNACLE**<sup>21</sup> validator is used within the system to validate the output dataset and define.xml based on the version selected by the user.



## Conclusion

How to handle different versions of SDTM & DEFINE generation in a Single Study?



The presentation was focused towards handling the different version of SDTM and Define-XML for a single study and went onto explain the details on how this can be done using a system in a more efficient, time save and consistent quality while dealing with such situations for many studies by a Sponsor or CRO.

There were many tools available and even the version comparison were provided by CDISC, which would involve manual effort by the users. The demonstration outlined with steps in this paper would facilitate ease of use in making such change for a study by a user and bring in a process framework to be followed by a CRO or a Sponsor who has global operations dealing with such situations across studies.

WE ARE DEDICATED  
TO THE FUTURE OF  
CLINICAL DEVELOPMENT  
AND TO EVERY  
LIFE IT IMPROVES.



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