Paper CD02

Generate Define.xml & Define.pdf from Metadata Environment

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ABSTRACT

The FDA requires a define file (CRT-DDS or define.xml) as a part of the Case Report Tabulation folder for eCTD submission. The define file can contain the metadata for both tabulation and analysis datasets. The XML schema used to define the expected structure is based on an extension to the CDISC Operational Data Model (ODM).

This paper describes the SAS functions which are used to add metadata from an external SDTM conversion specification sheet (e.g. excel or csv) into the metadata repository, extract metadata from that repository as an XML file, map the resulting XML file into SAS datasets and finally generate define.xml & define.pdf from the SAS datasets. These functions deploy SAS Open Metadata Architecture.

A centralized metadata repository facilitates exploitation of the metadata in the following ways:
- generating the define.xml or define.pdf
- comparing metadata across studies to ensure consistency
- metadata checks to ensure compliance to the SDTM standard

Creating the study definition upstream and utilizing metadata this way provides a powerful and robust method to achieve high quality and consistent SDTM datasets & define.xml.

INTRODUCTION

Define.xml (CRT-DDS)

Define.xml describes the content and structure of clinical data in a machine readable format. The XML schema used to define the expected structure of define.xml is based on an extension to the CDISC Operational Data Model (ODM). ODM is a specification of a standard XML schema for the interchange and archive of clinical trials data and metadata. ODM is vendor neutral and platform independent and is compatible with a wide range of current, legacy and emergent clinical trials systems.

Define.xml is specified in FDA's electronic submission (eSub) guidance and the electronic Common Technical Document (eCTD) documents. Therefore it is mandatory to include define.xml within the electronic submission of a clinical trial to FDA. The formal name of define.xml is **C**ase **R**eport **T**abulation **D**ata **D**efinition **S**pecification (CRT-DDS). This data definition specification provides a list of the datasets included in the submission along with a detailed description of the contents of each dataset.

The data definition specification can also be provided in a printable format (define.pdf) for the ease of the reviewers.

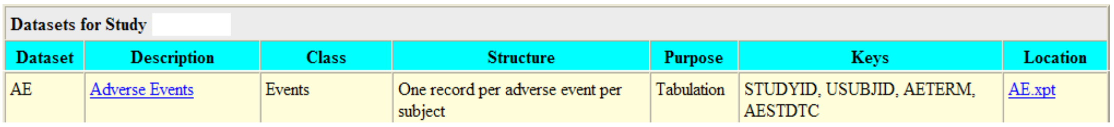
This paper describes a methodology to generate both define.xml and define.pdf from a common and centralized metadata repository. The define.xml can contain metadata for a wide range of standards including CDISC Study Data Tabulation Model (SDTM), CDISC Analysis Dataset Model (ADaM), and Standard for Exchange of Non-clinical Data (SEND). However, the scope of this paper is limited to CDISC SDTM.

CONTENTS OF DEFINE

The define.xml describes metadata at 5 Levels

1. Table level metadata
   The metadata at the table level consists of:
   - Name of the table
   - Description of the table
   - Class of the table
   - Structure of the table
   - Purpose of the table

- Keys of the table
- Location of the included XPT files.

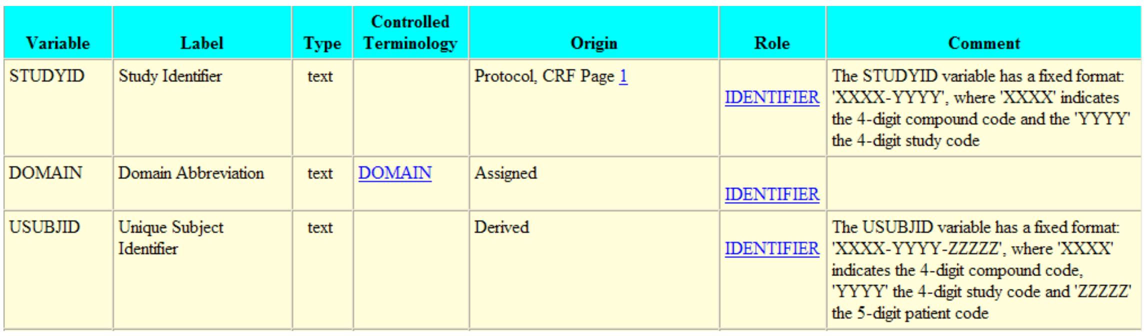


Datasets for Study

Dataset	Description	Class	Structure	Purpose	Keys	Location
AE	Adverse Events	Events	One record per adverse event per subject	Tabulation	STUDYID, USUBJID, AETERM, AESTDTC	AE.xpt

EXAMPLE OF TABLE LEVEL METADATA

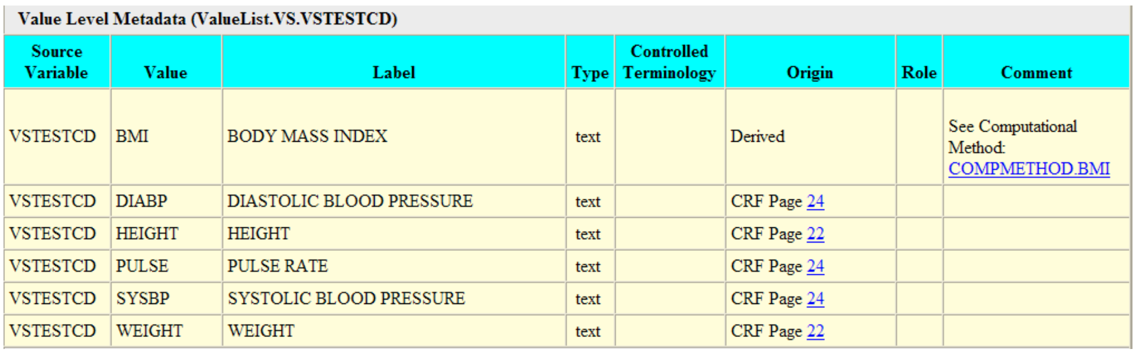
2. Variable level metadata
   The metadata at the variable level consists of:
   - Name of the variable
   - Label of the variable
   - Type of the variable
   - Controlled Terminology/Formats attached to the variable
   - Origin of the variable
   - Role of the variable
   - Comments for that variable (can also list the computational algorithm used to derive the variable)



Variable	Label	Type	Controlled Terminology	Origin	Role	Comment
STUDYID	Study Identifier	text		Protocol, CRF Page 1	IDENTIFIER	The STUDYID variable has a fixed format: 'XXXX-YYYY', where 'XXXX' indicates the 4-digit compound code and the 'YYYY' the 4-digit study code
DOMAIN	Domain Abbreviation	text	DOMAIN	Assigned	IDENTIFIER	
USUBJID	Unique Subject Identifier	text		Derived	IDENTIFIER	The USUBJID variable has a fixed format: 'XXXX-YYYY-ZZZZZ', where 'XXXX' indicates the 4-digit compound code, 'YYYY' the 4-digit study code and 'ZZZZZ' the 5-digit patient code

EXAMPLE OF VARIABLE LEVEL METADATA

3. Value level metadata
   The metadata at the value level consists of:
   - Name of the TESTCD/QNAM variable
   - Value of the TESTCD/QNAM i.e. TEST/QLABEL
   - Type of the value
   - Controlled Terminology/Formats attached to the value
   - Origin of the value
   - Role of the value
   - Comments for that value (can also list the computational algorithm used to derive the value)



Value Level Metadata (ValueList.VS.VSTESTCD)

Source Variable	Value	Label	Type	Controlled Terminology	Origin	Role	Comment
VSTESTCD	BMI	BODY MASS INDEX	text		Derived		See Computational Method: COMPMETHOD.BMI
VSTESTCD	DIABP	DIASTOLIC BLOOD PRESSURE	text		CRF Page 24		
VSTESTCD	HEIGHT	HEIGHT	text		CRF Page 22		
VSTESTCD	PULSE	PULSE RATE	text		CRF Page 24		
VSTESTCD	SYSBP	SYSTOLIC BLOOD PRESSURE	text		CRF Page 24		
VSTESTCD	WEIGHT	WEIGHT	text		CRF Page 22		

EXAMPLE OF VALUE LEVEL METADATA

4. Controlled Terminology metadata
   The metadata at the controlled terminology level consists of:
   - Controlled terminology name (Codelist/Format name)
   - Code value
   - Code text

SEX, Reference Name (SEX)	
Code Value	**Code Text**
F	FEMALE
M	MALE

EXAMPLE OF CONTROLLED TERMINOLOGY METADATA

5. Computational Algorithm metadata
   The metadata at computational algorithm level consists of:
   - Computational algorithm name
   - Name of the computational algorithm
   - Description of the computation method

Computational Algorithms (COMPMETHOD.AGE)	
Reference Name	**Computation Method**
COMPMETHOD.AGE	Equals to (DM.RFSTDTC-DM.BRTHDTC)/365.25

EXAMPLE OF COMPUTATIONAL ALGORITHM METADATA

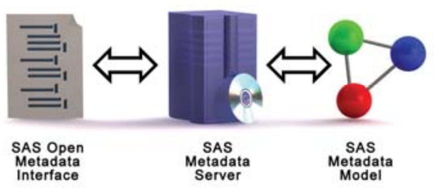
SAS OPEN METADATA ARCHITECTURE

The centralized metadata repository used to generate define.xml and define.pdf is based on SAS Open Metadata Architecture.

SAS Open Metadata Architecture is a general-purpose metadata management facility that provides common metadata services to SAS applications. The metadata architecture provides:

- SAS Metadata Server - provides a central location for storing metadata.
- SAS Open Metadata Interface - provides access to the server from a variety of programming environments, including Java, COM/DCOM, and SAS.
- SAS Metadata Model - provides a common, centralized method of searching and managing metadata.
- XML transport format and XML representation of metadata - makes it easy to transform the metadata to HTML and other standard XML representations, like the Object Management Group's Common Warehouse Metamodel (CWM).

The open metadata architecture enables users to perform metadata management tasks from a variety of programming environments such as Base SAS, SAS Data Integration Studio, and SAS Management Console. The PROC Metadata facility allows users to send XML requests to a metadata server to add, delete and update metadata. Users can also get metadata information in an XML format using PROC Metadata. The use of PROC Metadata to add/get metadata information is described in following sections.

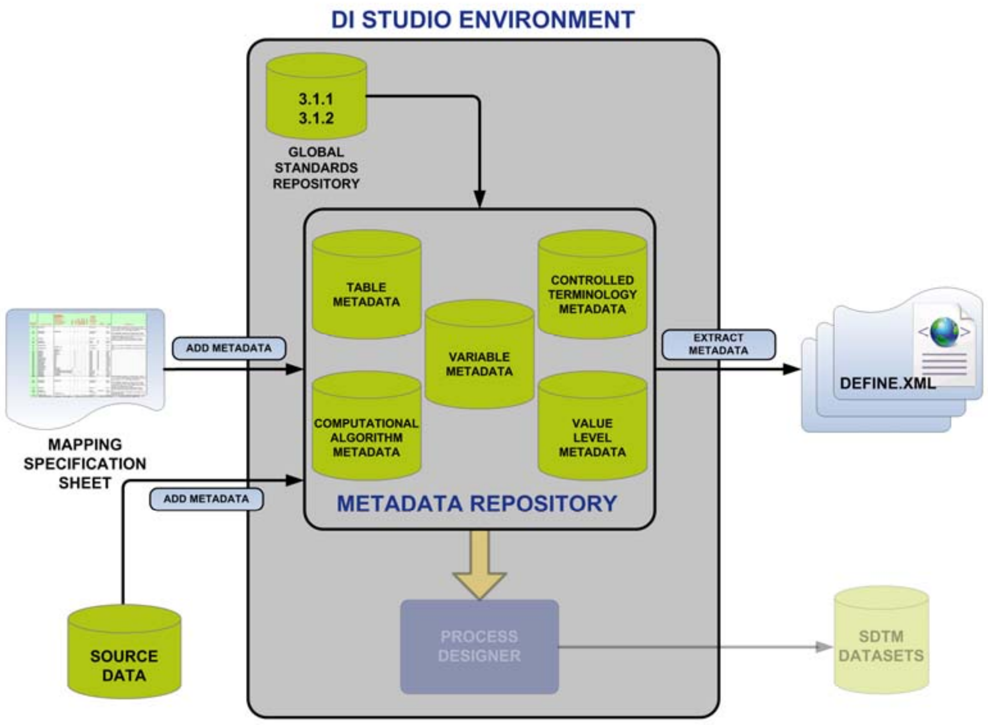


SAS OPEN METADATA ARCHITECTURE

GENERATE DEFINE.XML

GENERATING DEFINE.XML – METADATA PROCESS

The following diagram describes the process of creating define.xml and define.pdf from a centralized metadata repository.
The metadata for a particular clinical trial is described in a metadata specification sheet. The metadata is registered in the central metadata repository using the “<AddMetadata>” method. The centralized metadata repository stores metadata of all clinical trials related to a particular compound at one location.
The metadata is extracted from this repository using the “<GetMetadataObjects>” method.
The result is then converted into SAS datasets using SAS XML Mapper. These SAS datasets are used to generate define.xml and define.pdf using PROC Template and PROC Report respectively.

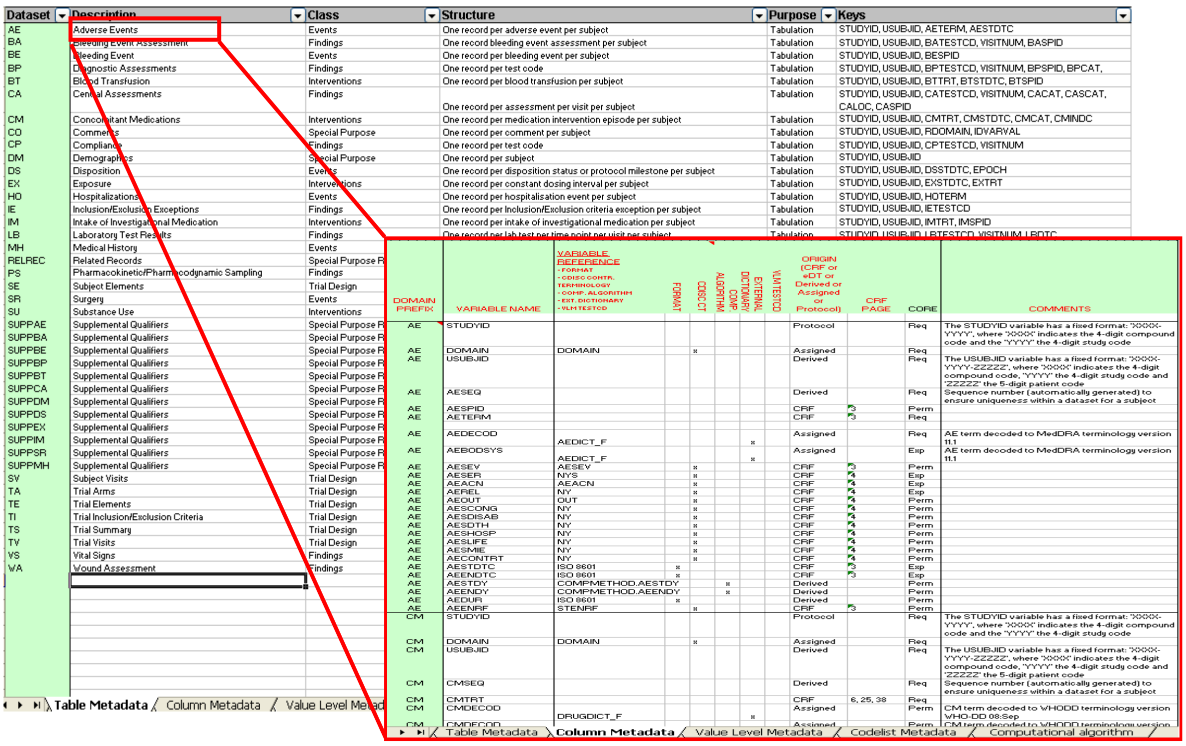


GENERATE DEFINE FROM CENTRALIZED METADATA REPOSITORY – METADATA PROCESS

The individual elements of the process are described as follows:

METADATA SPECIFICATION TABLE

The metadata specification table is the entry point of the process. The five levels of metadata – table metadata, variable metadata, value level metadata, controlled terminology and computational algorithms, as discussed earlier are defined in a mapping specification sheet. The metadata specification sheet can be in excel, text, CSV or any other format which SAS is able to import.



Dataset	Description	Class	Structure	Purpose	Keys
AE	Adverse Events	Events	One record per adverse event per subject	Tabulation	STUDYID, USUBJID, AETERM, AESTDTC
BA	Bleeding Event Assessment	Findings	One record bleeding event assessment per subject	Tabulation	STUDYID, USUBJID, BATESTCD, VISITNUM, BASPID
BE	Bleeding Event	Events	One record per bleeding event per subject	Tabulation	STUDYID, USUBJID, BESPID
BP	Diagnostic Assessments	Findings	One record per test code	Tabulation	STUDYID, USUBJID, BPTESTCD, VISITNUM, BPSPID, BPCAT,
BT	Blood Transfusion	Interventions	One record per blood transfusion per subject	Tabulation	STUDYID, USUBJID, BTTRT, BTSTDTC, BTSPID
CA	Central Assessments	Findings	One record per assessment per visit per subject	Tabulation	STUDYID, USUBJID, CATESTCD, VISITNUM, CACAT, CASCAT, CALOC, CASPID
CM	Concomitant Medications	Interventions	One record per medication intervention episode per subject	Tabulation	STUDYID, USUBJID, CMTRT, CMSTDTC, CMCAT, CMINDC
CO	Comments	Special Purpose	One record per comment per subject	Tabulation	STUDYID, USUBJID, RDOMAIN, IDVARVAL
CP	Compliance	Findings	One record per test code	Tabulation	STUDYID, USUBJID, CPTESTCD, VISITNUM
DM	Demographics	Special Purpose	One record per subject	Tabulation	STUDYID, USUBJID
DS	Disposition	Events	One record per disposition status or protocol milestone per subject	Tabulation	STUDYID, USUBJID, DSSTDTC, EPOCH
EX	Exposure	Interventions	One record per constant dosing interval per subject	Tabulation	STUDYID, USUBJID, EXSTDTC, EXTRT
HO	Hospitalizations	Events	One record per hospitalisation event per subject	Tabulation	STUDYID, USUBJID, HOTERM
IE	Inclusion/Exclusion Exceptions	Findings	One record per Inclusion/Exclusion criteria exception per subject	Tabulation	STUDYID, USUBJID, IETESTCD
IM	Intake of Investigational Medication	Interventions	One record per intake of investigational medication per subject	Tabulation	STUDYID, USUBJID, IMTRT, IMSPID
LB	Laboratory Test Results	Findings	One record per lab test per time point per visit per subject	Tabulation	STUDYID, USUBJID, LBTESTCD, VISITNUM, LBDTC
MH	Medical History	Events			
RELREC	Related Records	Special Purpose R			
PS	Pharmacokinetic/Pharmacodynamic Sampling	Findings			
SE	Subject Elements	Trial Design			
SR	Surgery	Events			
SU	Substance Use	Interventions			
SUPPAE	Supplemental Qualifiers	Special Purpose R			
SUPPBA	Supplemental Qualifiers	Special Purpose R			
SUPPBE	Supplemental Qualifiers	Special Purpose R			
SUPPBP	Supplemental Qualifiers	Special Purpose R			
SUPPBT	Supplemental Qualifiers	Special Purpose R			
SUPPCA	Supplemental Qualifiers	Special Purpose R			
SUPPDM	Supplemental Qualifiers	Special Purpose R			
SUPPDS	Supplemental Qualifiers	Special Purpose R			
SUPPEX	Supplemental Qualifiers	Special Purpose R			
SUPPIM	Supplemental Qualifiers	Special Purpose R			
SUPPSR	Supplemental Qualifiers	Special Purpose R			
SUPPMH	Supplemental Qualifiers	Special Purpose R			
SV	Subject Visits	Trial Design			
TA	Trial Arms	Trial Design			
TE	Trial Elements	Trial Design			
TI	Trial Inclusion/Exclusion Criteria	Trial Design			
TS	Trial Summary	Trial Design			
TV	Trial Visits	Trial Design			
VS	Vital Signs	Findings			
WA	Wound Assessment	Findings			

Table Metadata / Column Metadata / Value Level Metad

DOMAIN PREFIX	VARIABLE NAME	VARIABLE REFERENCE - FORMAT - CDISC CONTR. TERMINOLOGY - COMP. ALGORITHM - EXT. DICTIONARY - VLM TESTCD	FORMAT	CDISC CT	COMP. ALGORITHM	EXTERNAL DICTIONARY	VLM TESTCD	ORIGIN (CRF or eDT or Derived or Assigned or Protocol)	CRF PAGE	CORE	COMMENTS
AE	STUDYID							Protocol		Req	The STUDYID variable has a fixed format: 'XXXX-YYYY', where 'XXXX' indicates the 4-digit compound code and the 'YYYY' the 4-digit study code
AE	DOMAIN	DOMAIN		x				Assigned		Req	
AE	USUBJID							Derived		Req	The USUBJID variable has a fixed format: 'XXXX-YYYY-ZZZZZ', where 'XXXX' indicates the 4-digit compound code, 'YYYY' the 4-digit study code and 'ZZZZZ' the 5-digit patient code
AE	AESEQ							Derived		Req	Sequence number (automatically generated) to ensure uniqueness within a dataset for a subject
AE	AESPID							CRF	3	Perm	
AE	AETERM							CRF	3	Req	
AE	AEDECOD	AEDICT_F				x		Assigned		Req	AE term decoded to MedDRA terminology version 11.1
AE	AEBODSYS	AEDICT_F				x		Assigned		Exp	AE term decoded to MedDRA terminology version 11.1
AE	AESEV	AESEV		x				CRF	3	Perm	
AE	AESER	NYS		x				CRF	4	Exp	
AE	AEACN	AEACN		x				CRF	4	Exp	
AE	AEREL	NY		x				CRF	4	Exp	
AE	AEOUT	OUT		x				CRF	4	Perm	
AE	AESCONG	NY		x				CRF	4	Perm	
AE	AESDISAB	NY		x				CRF	4	Perm	
AE	AESDTH	NY		x				CRF	4	Perm	
AE	AESHOSP	NY		x				CRF	4	Perm	
AE	AESLIFE	NY		x				CRF	4	Perm	
AE	AESMIE	NY		x				CRF	4	Perm	
AE	AECONTRT	NY		x				CRF	4	Perm	
AE	AESTDTC	ISO 8601	x					CRF	3	Exp	
AE	AEENDTC	ISO 8601	x					CRF	3	Exp	
AE	AESTDY	COMPMETHOD.AESTDY			x			Derived		Perm	
AE	AEENDY	COMPMETHOD.AEENDY			x			Derived		Perm	
AE	AEDUR	ISO 8601	x					Derived		Perm	
AE	AEENRF	STENRF		x				CRF	3	Perm	
CM	STUDYID							Protocol		Req	The STUDYID variable has a fixed format: 'XXXX-YYYY', where 'XXXX' indicates the 4-digit compound code and the 'YYYY' the 4-digit study code
CM	DOMAIN	DOMAIN		x				Assigned		Req	
CM	USUBJID							Derived		Req	The USUBJID variable has a fixed format: 'XXXX-YYYY-ZZZZZ', where 'XXXX' indicates the 4-digit compound code, 'YYYY' the 4-digit study code and 'ZZZZZ' the 5-digit patient code
CM	CMSEQ							Derived		Req	Sequence number (automatically generated) to ensure uniqueness within a dataset for a subject
CM	CMTRT							CRF	6, 25, 38	Req	
CM	CMDECOD	DRUGDICT_F				x		Assigned		Perm	CM term decoded to WHODD terminology version WHO-DD 08:Sep
CM	CMDECOD							Assigned		Perm	CM term decoded to WHODD terminology version

Table Metadata / Column Metadata / Value Level Metadata / Codelist Metadata / Computational algorithm

EXAMPLE METADATA SPECIFICATION SHEET

ADD METADATA

The next step is to add the metadata defined in the metadata specification sheet to the centralized metadata repository. Since the repository is based on SAS open metadata architecture, it has an XML transport engine. Therefore to add metadata to the metadata repository, requests are sent to the server in a XML format. The XML string is constructed keeping in mind the rules of SAS metadata model.

This is a snippet of the program used to Add Metadata in the centralized repository.

```
%Macro Addtablemetadata (Extension =, Value=, TableId =);
data _null_;
File addmeta;
PUT  '<AddMetadata>';
PUT  '<Metadata>';
PUT  "<Extension Id    = " """"""";
PUT  "            Name  = " """&Extension""";
PUT  "            Value = " """&Value""" ">";
PUT  '<owningobject>';
PUT  "  <PhysicalTable objref= " """&TableId""" "/>";
PUT  '</owningobject>';
PUT  '</Extension>';
PUT  '</Metadata>';
PUT  '<Reposid>$METAREPOSITORY</Reposid>';
PUT  '       <NS>SAS</NS>';
PUT  '<Flags>268435456</Flags>';
PUT  '<Options/>';
PUT  '</AddMetadata>';
Run;

Proc Metadata Repos = "&REP_ID."  In = addmeta;
Run;

%Mend Addtablemetadata;
```

The key points to note in this program are the <AddMetadata> method and PROC METADATA procedure.
In the example, <AddMetadata> is the method name and <Metadata>, <Reposid>, <NS>, <Flags>, <Options> are AddMetadata parameters. The XML elements that are nested within the <Metadata></Metadata> tags comprise a metadata property string that defines the metadata object to be added.

The metadata of all clinical trials for a particular compound can be added to this central metadata repository. The <AddMetadata> call can be issued from a variety of programming environments as long as the programming environment is based on SAS Open Metadata Architecture.

GET METADATA

The next step is to extract desired metadata from the metadata repository. For extracting the metadata, <GetMetadataObjects> method is used. <XMLSelect> search string is used to extract the relevant metadata. The GetMetadata request is sent to the SAS metadata server using PROC Metadata.

Listed below is a snippet of the program used to get metadata information from the centralized repository:

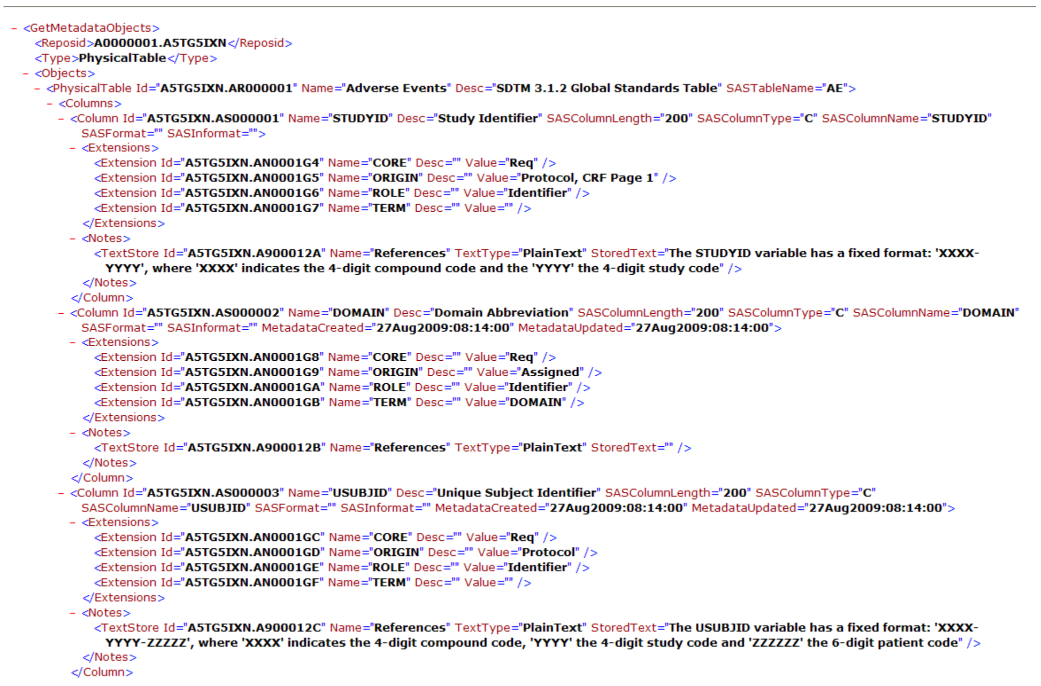
```
FILENAME INPUT TEMP;
FILENAME OUTPUT "…\output.xml";

data _null_;
file Input;
        put '<GetMetadataObjects>';
        put '<Reposid>$METAREPOSITORY</Reposid>';
        put '<Type>PhysicalTable</Type>';
        put '<Objects/>';
        put '<NS>SAS</NS>';
        put '<Flags>388</Flags>';
        put '<Options>';
        put '<XMLSelect search="PhysicalTable[@SASTableName = '@;
        put "'" "&NAME" "']/TablePackage/SASLibrary[@Libref = " @;
        put "'" "&libref" "'" @;
        put ']]"/>';
        put '<Templates>';
        put '<PhysicalTable Id="" Name="" Desc="" SASTableName="" >';
        put '<Columns/>';
        put '<Extensions/>';
        put '<Notes/>';
        put '</PhysicalTable>';
        put '<Column ID="" Name="" Desc="" SASColumnLength="" SASColumnType=""';
        put '                SASColumnName="" SASFormat="" SASInformat="">';
        put '                <Extensions/>  <Notes/>  </Column>';
        put '<Extension ID="" Name="" Desc="" Value=""/>';
        put ' <TextStore ID="" Name="" TextType="" StoredText="" />';
        put '    </Templates>';
        put '   </Options>';
        put '</GetMetadataObjects>';run;

Proc Metadata Repos = "&Rep_ID." in=input out=results;
run;
```

The <Reposid> element identifies the repository to query. The <type> element identifies the type of the metadata object to query. The metadata objects that were found are listed in the <Objects> element. The structure of the resulting xml file is determined by the <Templates> attribute. The <XMLSelect> element enables passing a search string to the server. In this example a physical table is queried. The result of the above program is returned in an xml file (filename “results”).

The result.xml is as shown in the diagram below:



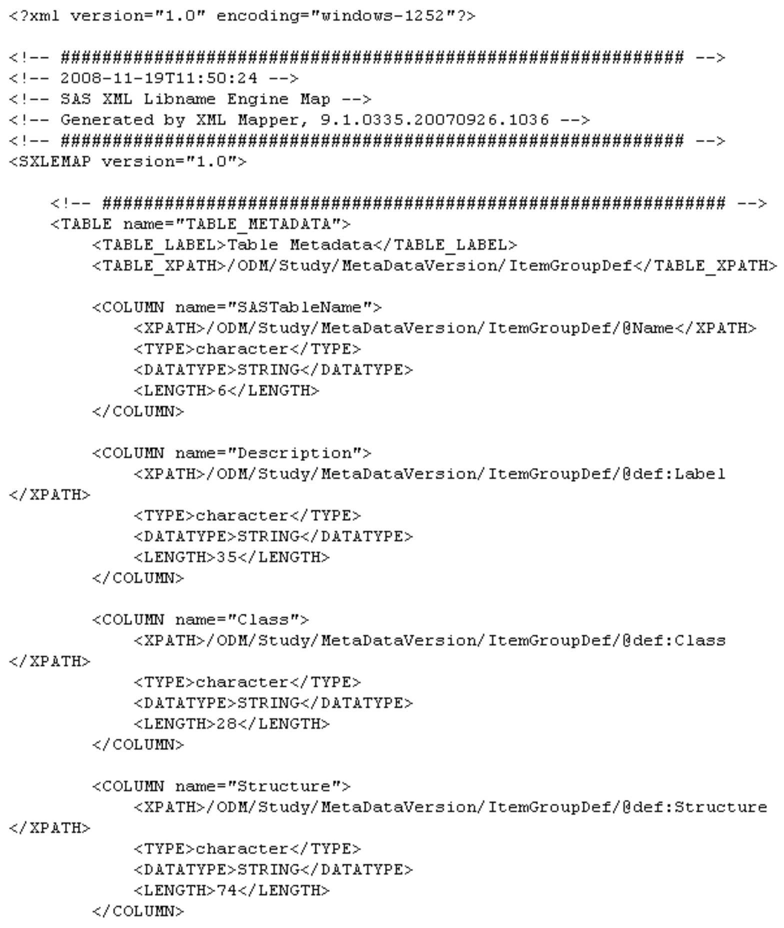
```
- <GetMetadataObjects>
    <Reposid>A0000001.A5TG5IXN</Reposid>
    <Type>PhysicalTable</Type>
  - <Objects>
    - <PhysicalTable Id="A5TG5IXN.AR000001" Name="Adverse Events" Desc="SDTM 3.1.2 Global Standards Table" SASTableName="AE">
      - <Columns>
        - <Column Id="A5TG5IXN.AS000001" Name="STUDYID" Desc="Study Identifier" SASColumnLength="200" SASColumnType="C" SASColumnName="STUDYID"
            SASFormat="" SASInformat="">
          - <Extensions>
              <Extension Id="A5TG5IXN.AN0001G4" Name="CORE" Desc="" Value="Req" />
              <Extension Id="A5TG5IXN.AN0001G5" Name="ORIGIN" Desc="" Value="Protocol, CRF Page 1" />
              <Extension Id="A5TG5IXN.AN0001G6" Name="ROLE" Desc="" Value="Identifier" />
              <Extension Id="A5TG5IXN.AN0001G7" Name="TERM" Desc="" Value="" />
            </Extensions>
          - <Notes>
              <TextStore Id="A5TG5IXN.A900012A" Name="References" TextType="PlainText" StoredText="The STUDYID variable has a fixed format: 'XXXX-
                YYYY', where 'XXXX' indicates the 4-digit compound code and the 'YYYY' the 4-digit study code" />
            </Notes>
          </Column>
        - <Column Id="A5TG5IXN.AS000002" Name="DOMAIN" Desc="Domain Abbreviation" SASColumnLength="200" SASColumnType="C" SASColumnName="DOMAIN"
            SASFormat="" SASInformat="" MetadataCreated="27Aug2009:08:14:00" MetadataUpdated="27Aug2009:08:14:00">
          - <Extensions>
              <Extension Id="A5TG5IXN.AN0001G8" Name="CORE" Desc="" Value="Req" />
              <Extension Id="A5TG5IXN.AN0001G9" Name="ORIGIN" Desc="" Value="Assigned" />
              <Extension Id="A5TG5IXN.AN0001GA" Name="ROLE" Desc="" Value="Identifier" />
              <Extension Id="A5TG5IXN.AN0001GB" Name="TERM" Desc="" Value="DOMAIN" />
            </Extensions>
          - <Notes>
              <TextStore Id="A5TG5IXN.A900012B" Name="References" TextType="PlainText" StoredText="" />
            </Notes>
          </Column>
        - <Column Id="A5TG5IXN.AS000003" Name="USUBJID" Desc="Unique Subject Identifier" SASColumnLength="200" SASColumnType="C"
            SASColumnName="USUBJID" SASFormat="" SASInformat="" MetadataCreated="27Aug2009:08:14:00" MetadataUpdated="27Aug2009:08:14:00">
          - <Extensions>
              <Extension Id="A5TG5IXN.AN0001GC" Name="CORE" Desc="" Value="Req" />
              <Extension Id="A5TG5IXN.AN0001GD" Name="ORIGIN" Desc="" Value="Protocol" />
              <Extension Id="A5TG5IXN.AN0001GE" Name="ROLE" Desc="" Value="Identifier" />
              <Extension Id="A5TG5IXN.AN0001GF" Name="TERM" Desc="" Value="" />
            </Extensions>
          - <Notes>
              <TextStore Id="A5TG5IXN.A900012C" Name="References" TextType="PlainText" StoredText="The USUBJID variable has a fixed format: 'XXXX-
                YYYY-ZZZZZ', where 'XXXX' indicates the 4-digit compound code, 'YYYY' the 4-digit study code and 'ZZZZZZ' the 6-digit patient code" />
            </Notes>
          </Column>
```

RESULT.XML

The next step is to convert the result.xml output file into SAS Datasets.

MAP XML TO SAS DATASETS

The conversion of result.xml output file into SAS datasets is achieved with the help of a map file generated by SAS XML Mapper. Since the xml structure of result.xml is always the same (as determined by the <template> element in the previous step) the map file needs to be generated just once and it will always convert result.xml into the required SAS Datasets.



```
<?xml version="1.0" encoding="windows-1252"?>

<!-- ############################################################ -->
<!-- 2008-11-19T11:50:24 -->
<!-- SAS XML Libname Engine Map -->
<!-- Generated by XML Mapper, 9.1.0335.20070926.1036 -->
<!-- ############################################################ -->
<SXLEMAP version="1.0">

    <!-- ############################################################ -->
    <TABLE name="TABLE_METADATA">
        <TABLE_LABEL>Table Metadata</TABLE_LABEL>
        <TABLE_XPATH>/ODM/Study/MetaDataVersion/ItemGroupDef</TABLE_XPATH>

        <COLUMN name="SASTableName">
            <XPATH>/ODM/Study/MetaDataVersion/ItemGroupDef/@Name</XPATH>
            <TYPE>character</TYPE>
            <DATATYPE>STRING</DATATYPE>
            <LENGTH>6</LENGTH>
        </COLUMN>

        <COLUMN name="Description">
            <XPATH>/ODM/Study/MetaDataVersion/ItemGroupDef/@def:Label
</XPATH>
            <TYPE>character</TYPE>
            <DATATYPE>STRING</DATATYPE>
            <LENGTH>35</LENGTH>
        </COLUMN>

        <COLUMN name="Class">
            <XPATH>/ODM/Study/MetaDataVersion/ItemGroupDef/@def:Class
</XPATH>
            <TYPE>character</TYPE>
            <DATATYPE>STRING</DATATYPE>
            <LENGTH>28</LENGTH>
        </COLUMN>

        <COLUMN name="Structure">
            <XPATH>/ODM/Study/MetaDataVersion/ItemGroupDef/@def:Structure
</XPATH>
            <TYPE>character</TYPE>
            <DATATYPE>STRING</DATATYPE>
            <LENGTH>74</LENGTH>
        </COLUMN>
```

EXAMPLE MAP FILE GENERATED BY SAS XML MAPPER

Once the map file is generated the following piece of code converts the resulting xml file into SAS Datasets

```
   filename myxmlmap "&define.\tempdata\tablemetadata.map";
   libname tempdata xml xmlmap=myxmlmap xmlfileref=results;

   Proc Copy in = tempdata out = work;
   Run;
```

In the program, filename “myxmlmap” is given to the map file. An xml library “tempdata” is defined and the name of the map file and the output file “result.xml” is specified in the options. The PROC Copy procedure copies all the datasets from the XML library into the work library. These SAS Datasets can be manipulated to generate define.xml & define.pdf.

PROC TEMPLATE

Proc Template can be used to generate define.xml from the resulting SAS Datasets created in the previous step. The event functionality in PROC Template makes dynamic templates. Various events can be triggered based on conditions in the dataset. Then theses dynamic templates write XML tags according to the data present.

Listed below is a snippet of the program used to generate define.xml from SAS Datasets

```
Proc template;
Define tagset TMP.ComputationMethod;

parent = tagsets.sasxmog;
Notes "SAS XML Engine tagsets for SDTM ComputationMethod";

/*     define and initialize variables */
       mvar markup
            OID
            ItemOID;
       define event row;
              start:
                     break;
              finish:
                     do /if cmp($markup, "FIRST");
                            trigger markupFirst;
                     else /if cmp ($markup, "COMMENT");
                            trigger writeComment;
                     done;
                     break;
       end;

/* Use SASColumn event to load values into variables*/
       define event SASColumn;
              start:
                     break;
              finish:
                     do /if cmp(NAME, "MARKUP");
                            set $markup VALUE;
                            break;
                     else /if cmp(NAME, "OID");
                            set $OID VALUE;
                            break;
                     else /if cmp (NAME, "ITEMOID");
                            set $ItemOID VALUE;
                     done;
                     break;
                     end;

/* Define Tag writing events */

       define event writeStart;
              putq "<def:ComputationMethod OID=" $OID ">" CR;
       break;
       end;

       define event writeEnd;
              put "</def:ComputationMethod>" CR;
       break;
       end;

       define event writeMid;
              put $ItemOID CR;
              break;
       end;

       define event writeComment;
              put "<!--" $ItemOID "-->" CR;
              break;
       end;

       define event markupFirst;
                     put NL;
                     trigger writeStart;
                     trigger writeMid;
                     trigger writeEnd;
              break;
              end;

       end;
       run;
```

For the five different levels of metadata, five different templates would be needed. Two additional templates would be needed for header & footer information. The PROC Template would then create seven different individual xml files. These seven xml files could be combined to generate a complete define.xml.

PROC REPORT

PROC Report is used to generate define.pdf from the resulting SAS Datasets. The compute block can be used to generate hyperlinks within the define.pdf. The ODS option PROCLABEL and PROC Report option PROC Contents enable good control over bookmarks. However, external pdf procedures could be used to gain complete control over bookmarks. Kindly see the references for further information on moving and splitting bookmarks.

Listed below is a snippet of the program used to generate define.pdf from SAS Datasets.

```
ODS PROCLABEL = "Datasets for Study &STUDY_ID.";
PROC REPORT DATA=Table_Metadata nowd noheader nocenter SPLIT=' ' CONTENTS="SDTM Domains"
style(report) = [OUTPUTWIDTH = 100%];

columns SASTableName DESCRIPTION CLASS STRUCTURE PURPOSE KEYS XPORT;

define SASTableName/display width=30 "Dataset";
define DESCRIPTION/display width=30 "Description";
define CLASS/display width=10 "Class" ;
define STRUCTURE/display width=40 "Structure";
define PURPOSE/display width=40 "Purpose" ;
define KEYS/display width=30 "Keys" ;
define XPORT/display "Location" ;

COMPUTE XPORT;
URLSTRING = STRIP(XPORT);
CALL DEFINE (_COL_, 'URL', URLSTRING);
ENDCOMP;

RUN;
```

To generate all five levels of metadata five separate PROC Report procedures are needed. The compute block can also be used to color headers differently and also to generate page numbers.

CONCLUSION

The key concept in the methodology presented above is a centralized metadata repository.
The centralized metadata repository integrates all the metadata and stores it in one meta model schema that can be accessed easily. The following are the advantages of a centralized metadata repository:

- Efficiently generate define.xml & define.pdf.
- Run metadata validation checks on the repository to ensure high quality of metadata.
- Compare metadata to ensure consistency across all trials and facilitate cross study analysis.
- Create actual SDTM datasets based on the metadata definition provided in the central repository.
- Metadata repository populated before actual programming begins, so SDTM metadata available to statisticians without actual SDTM datasets.

Creating the study definition upstream and utilizing metadata this way provides a powerful and robust method to achieve high quality and consistent SDTM datasets & define.xml, ensuring a successful submission.

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