



# HOW TO CREATE YOUR DEFINE.XML AS EARLY AS POSSIBLE WITH A CLICK ON A BUTTON

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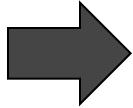
SGS - Agriculture, Food and Life, Life Sciences - Clinical Research

WHEN YOU NEED TO BE SURE



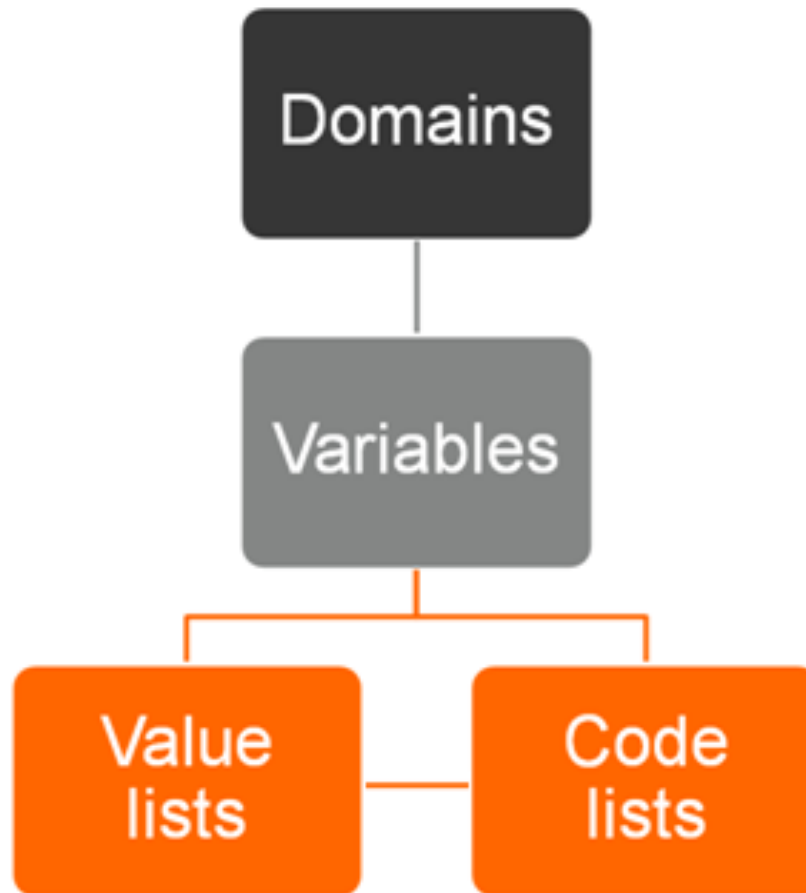
- Define.xml
  - Data definition specification
  - Metadata for SDTM, SEND and ADaM
  - Submission to regulatory agencies indicating the datasets, variables, controlled terms, and other specified metadata used
- Define.xml creation can be a difficult task
  - Manual operations can lead to errors
  - Living document, a lot of maintenance

- Automated creation and maintenance of the Define.xml
  - in-house developed applications



- Reduce manual operations
- Provide accurate Define.xml

- Master source of metadata, global metadata library
- Based on SDTM structure
- Contains all available
  - Domains
  - Variables
  - Value lists
  - Code lists
  - Computational Methods
- Different MDR versions
  - Sponsor specific implementation
  - New implementation version



- Define.xml
  - Start with complete master metadata library
  - Copy MDR at trial level
  - Make it more trial specific

Domains

MDR

|        |        |
|--------|--------|
| CM     | VS     |
| SUPPCM | EG     |
| LB     | SUPPEG |
| SUPPLB |        |
| DS     | SUPPDM |
| SUPPDS |        |

Trial

|    |        |
|----|--------|
| DM | RELREC |
| TA | EX     |
| AE | SUPPEX |

Domains

Variables

Value  
lists

Code  
lists

Variables

MDR - DM

|         |         |
|---------|---------|
| RFSTDTC | RACE    |
| RFENDTC | ETHNIC  |
| DTHDTC  | BRTHDTC |
| SITEID  |         |
| INVNAM  |         |
| SUPPDS  |         |

Trial

|         |        |
|---------|--------|
| STUDYID | SUBJID |
| DOMAIN  | AGE    |
| USUBJID | SEX    |
| ARMCD   |        |

Domains

Variables

Value  
lists

Code  
lists

## Database view

| DATASET | DESCRIPTION                   | CLASS           | STRUCTURE                                                   |
|---------|-------------------------------|-----------------|-------------------------------------------------------------|
| TA      | Trial Arms                    | Trial Design    | One record per planned Element per Arm                      |
| DM      | Demographics                  | Special-Purpose | One record per subject                                      |
| CM      | Concomitant/Prior Medications | Interventions   | One record per recorded intervention occurrence or const... |
| EX      | Exposure                      | Interventions   | One record per protocol-specified study treatment, const... |

| PURPOSE    | KEYS                                                | DSORDER | SGSSTATE |
|------------|-----------------------------------------------------|---------|----------|
| Tabulation | STUDYID, ARMCD, TAETORD                             | 001     | IN       |
| Tabulation | STUDYID, USUBJID                                    | 009     | IN       |
| Tabulation | STUDYID, USUBJID, CMTRT, CMSTDTC, CMSCAT            | 013     | EX       |
| Tabulation | STUDYID, USUBJID, EXTRT, EXSTDTC, EXTPTNUM, EXREFID | 015     | IN       |

## SGSSTATE: IN, EX

■ Define.xml

**Tabulation Datasets for Study SGSTRIAL (SDTM 3.2) (SDTM-IG 3.2)**

| Dataset | Description                                    | Class           | Structure                                                                                | Purpose    | Keys                                              | Location                   |
|---------|------------------------------------------------|-----------------|------------------------------------------------------------------------------------------|------------|---------------------------------------------------|----------------------------|
| TA      | <a href="#">Trial Arms</a>                     | Trial Design    | One record per planned Element per Arm                                                   | Tabulation | STUDYID, ARMCD, TAETORD                           | <a href="#">TA.xpt</a>     |
| DM      | <a href="#">Demographics</a>                   | Special-Purpose | One record per subject                                                                   | Tabulation | STUDYID, USUBJID                                  | <a href="#">DM.xpt</a>     |
| EX      | <a href="#">Exposure</a>                       | Interventions   | One record per protocol-specified study treatment, 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, AETERM, AESTDTC                 | <a href="#">AE.xpt</a>     |
| RELREC  | <a href="#">Related Records</a>                | Relationship    | One record per related record, group of records or dataset                               | Tabulation | STUDYID, RDOMAIN, USUBJID, IDVAR, IDVARVAL, RELID | <a href="#">RELREC.xpt</a> |
| SUPPEX  | <a href="#">Supplemental Qualifiers for EX</a> | Relationship    | One record per IDVAR, IDVARVAL and QNAM per subject                                      | Tabulation | STUDYID, RDOMAIN, USUBJID, IDVAR, IDVARVAL, QNAM  | <a href="#">SUPPEX.xpt</a> |

Go to the [top](#) of the define.xml

- Automatically make the MDR trial specific
  - Annotation Tool
  - SDTM Mapping Tool

## IN-HOUSE DEVELOPED APPLICATIONS: ANNOTATION TOOL

- Guide user in annotating a CRF
  - Copy from annotation library
  - Guidance in new annotations
  - Layout of annotations
  - Review process
  - Customisable per implementation standard
  - Future proof: new implementation standards
- Oracle Application Express

044. ----- Demographics 1.....|.....43|.....16|.....



[DM - Demographics]

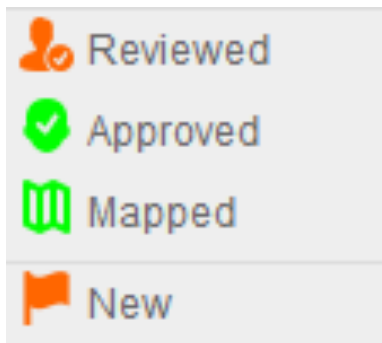
## Demographics 1

|  |               |              |                                                                                                                                                                                                                                         |
|--|---------------|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  | Date of birth | DM1.DOB<br>T | <b>BRTHDTC</b>                                                                                                                                                                                                                          |
|  | Sex at birth  | DM1.SEX      | <input type="radio"/> Male<br><input type="radio"/> Female <b>SEX</b>                                                                                                                                                                   |
|  | Race          | DM1.RACE     | <input type="radio"/> Not allowed to ask as per local regulations<br><input type="radio"/> Please specify: <b>RACE = NOT ALLOWED TO ASK AS PER LOCAL REGULATIONS</b>                                                                    |
|  | Specify race: | DM1.RACES    | <input type="text"/> <b>RACE</b>                                                                                                                                                                                                        |
|  | Ethnicity     | DM1.ETHN     | <input type="radio"/> Not allowed to ask per local regulations<br><input type="radio"/> Hispanic or Latino<br><input type="radio"/> Not Hispanic or Latino <b>ETHNIC = NOT ALLOWED TO ASK AS PER LOCAL REGULATIONS</b><br><b>ETHNIC</b> |

## IN-HOUSE DEVELOPED APPLICATIONS: ANNOTATION TOOL

roman\_radelicki

- PDF is uploaded and available in the tool
- Look and feel of the annotations
  - Font, font size, color linked to specific implementation standard
- Review process



The screenshot displays the SGS annotation tool interface. At the top, there is a search bar with the text "43|16|". Below the search bar is a toolbar with various icons for document manipulation. The main form area contains several fields for data entry and annotation:

- M1.DOB**: A text input field with the value "BRTHDTC".
- M1.SEX**: A radio button selection for "Male" or "Female", with an annotation "SEX" next to it.
- M1.RACE**: A radio button selection for "Not allowed to ask as per local regulations" or "Please specify:", with an annotation "RACE = NOT ALLOWED TO ASK AS PER LOCAL REGULATIONS" next to it.
- M1.RACES**: A dropdown menu with an "ADD" button, with an annotation "RACE" next to it.
- M1.ETHN**: A radio button selection for "Not allowed to ask per local regulations", "Hispanic or Latino", or "Not Hispanic or Latino", with an annotation "ETHNIC = NOT ALLOWED TO ASK AS PER LOCAL REGULATIONS" next to it.

A legend on the left side of the form shows four status icons: "Reviewed" (orange person icon), "Approved" (green checkmark icon), "Mapped" (green book icon), and "New" (orange flag icon).

## IN-HOUSE DEVELOPED APPLICATIONS: ANNOTATION TOOL

### ADD ANNOTATION

Annotation type

TESTCD.....#DOMAIN#ORRES when #DOMAIN#TESTCD = #FINDING#

Domain

VS.....Vital Signs

Finding

MUARMCIR.....Mid-Upper Arm Circumference  
 OXYSAT.....Oxygen Saturation  
 PULSE.....Pulse Rate  
 PULSE.....Pulse Rate  
 PULSEPR.....Pulse Pressure  
 RESP.....Respiratory Rate  
 SAD.....Sagittal Abdominal Diameter  
 SSSKNF.....Subscapular Skinfold Thickness  
 SYSBP.....Systolic Blood Pressure  
 TBW.....Total Body Water  
 TEMP.....Temperature  
 TRSKNF.....Triceps Skinfold Thickness  
 VSALL.....All Vital Signs (not approved)  
**WEIGHT.....Weight**  
 WSTCIR.....Waist Circumference

# IN-HOUSE DEVELOPED APPLICATIONS: ANNOTATION TOOL

tool

[roman\\_radelicki](#) [Feedback](#) [Switch app](#) [Log](#)

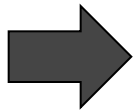
Go

Actions ▾

| Annottype     | Textfont | Objecttype | Fillcolor | Annotcolor | Annotformat                                              | Fontweight | Fonttype | Textsize |
|---------------|----------|------------|-----------|------------|----------------------------------------------------------|------------|----------|----------|
| VARIABLE      | Arial    | FreeText   | -         | #0000FF    | <b>#VARNAME#</b>                                         | bold       | italic   | 11       |
| SUPP          | Arial    | FreeText   | -         | #FF0000    | <b>SUPP#DOMAIN#.QVAL when<br/>QNAM = #QNAM#</b>          | bold       | italic   | 11       |
| TESTCD        | Arial    | FreeText   | -         | #0000FF    | <b>#DOMAIN#ORRES when<br/>#DOMAIN#TESTCD = #FINDING#</b> | bold       | italic   | 11       |
| NOT_SUBMITTED | Arial    | FreeText   | -         | #0000FF    | <b>[Not submitted]</b>                                   | bold       | italic   | 11       |

## IN-HOUSE DEVELOPED APPLICATIONS: ANNOTATION TOOL

- More accurate and qualitative annotated eCRF
- Annotations captured electronically
  - Use in other applications e.g. Define.xml



- Domains, variables, values lists, code lists used in the annotation are known
- Make metadata more specific by setting the SGSSTATE flag in the MDR

| DATASET | DESCRIPTION                   | CLASS           | SGSSTATE |
|---------|-------------------------------|-----------------|----------|
| TA      | Trial Arms                    | Trial Design    | IN       |
| DM      | Demographics                  | Special-Purpose | IN       |
| CM      | Concomitant/Prior Medications | Interventions   | EX       |
| EX      | Exposure                      | Interventions   | IN       |

## IN-HOUSE DEVELOPED APPLICATIONS: SDTM MAPPING TOOL

- Based on annotation tool and on applicable MDR, mapping is performed by the programmer
- EDC extracts (usually SAS<sup>TM</sup> files), are loaded into the database
  - All input fields, radio buttons, checkboxes from the eCRF are captured and presented to the programmer like a pivot table
  - Per form the programmer is able to map each column to a specific SDTM variable
- Guide the programmer
  - Copy the complete mapping from another trial
  - Create a new mapping by selecting the applicable domain and variable from a standard specific dropdown list
- C# with Oracle database

## IN-HOUSE DEVELOPED APPLICATIONS: SDTM MAPPING TOOL

| File    | Edit     | Search          | Filter  | Window     | Help        |                 |      |      |          |
|---------|----------|-----------------|---------|------------|-------------|-----------------|------|------|----------|
| Mapping | Visitmap | Repeatingvisits | Patient | PreProcess | PostProcess | AfterConversion | DBMF | Data | Errorlog |

| FORMREFNAME | CCCONTROLREFNAME | FINDING | DOMAIN | TARGET  | PARAM1 | PARAM2 | P1 | P2 | P3 |
|-------------|------------------|---------|--------|---------|--------|--------|----|----|----|
| DM1         | ETHN_DEC         | N       | DM     | ETHNIC  |        |        |    |    |    |
| DM1         | DOBDT            | N       | DM     | BRTHDTC |        |        |    |    |    |
| DM1         | SEX              | N       | DM     | SEX     |        |        |    |    |    |
| DM1         | RACE             | N       | DM     | RACE    |        |        |    |    |    |

| P1 | P2 | P3 | CONVERTTYPE | CODE                                                                                |
|----|----|----|-------------|-------------------------------------------------------------------------------------|
|    |    |    | ANY         | case when CTSS\$ITEM = 'Not allowed to ask per local regulations' then 'NOT ALLOWED |
|    |    |    | VALUE       | upper(CTSS\$ITEM)                                                                   |
|    |    |    | FIRSTCHAR   | substr(upper(CTSS\$ITEM),1,1)                                                       |
|    |    |    | ANY         | case when upper(CTSS\$ITEM) in ('NATA') then 'NOT ALLOWED TO ASK AS PER LOCAL R     |

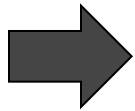
## IN-HOUSE DEVELOPED APPLICATIONS: SDTM MAPPING TOOL

### Demographics 1

|                                                                                  |               |              |                                                                                                                                                            |                                                                                                                                                                                                                                                            |
|----------------------------------------------------------------------------------|---------------|--------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  | Date of birth | DM1.DOB<br>T | <input type="text"/>                                                                                                                                       |  <b>BRTHDTC</b>                                                                                                                                                         |
|  | Sex at birth  | DM1.SEX      | <input type="radio"/> Male<br><input type="radio"/> Female                                                                                                 |  <b>SEX</b>                                                                                                                                                             |
|  | Race          | DM1.RACE     | <input type="radio"/> Not allowed to ask as per local regulations<br><input type="radio"/> Please specify:                                                 |  <b>RACE = NOT ALLOWED TO ASK AS PER LOCAL REGULATIONS</b>                                                                                                              |
|  | Specify race: | DM1.RACES    | <input type="text"/>                                                    |  <b>RACE</b>                                                                                                                                                            |
|  | Ethnicity     | DM1.ETHN     | <input type="radio"/> Not allowed to ask per local regulations<br><input type="radio"/> Hispanic or Latino<br><input type="radio"/> Not Hispanic or Latino |  <b>ETHNIC = NOT ALLOWED TO ASK AS PER LOCAL REGULATIONS</b><br><br> <b>ETHNIC</b> |

## THE KEY TO A COMPLETE DEFINE.XML

- Use an EDC test environment
- Enter test data with all possible questions and answers populated on the CRF



This test data + the in-house developed applications will enable us to create a Define.xml from study start



# THE KEY TO A COMPLETE DEFINE.XML

- Automatically populate SGSSTATE
  - Include or exclude domains, variables
- Origin of variables
- CRF page

| DATASET | VARNAME | VARLABEL                  | DATATYPE | LNTH | ORIGIN   | VARROLE          | CORE | VARORDER | CODELST | VALUEOID | CRFPAGE | SGSSTATE |
|---------|---------|---------------------------|----------|------|----------|------------------|------|----------|---------|----------|---------|----------|
| DM      | STUDYID | Study Identifier          | text     | 40   | Protocol | Identifier       | Req  | 001      |         |          |         | IN       |
| DM      | DOMAIN  | Domain Abbreviation       | text     | 2    | Assigned | Identifier       | Req  | 002      | DOMAIN  |          |         | IN       |
| DM      | USUBJID | Unique Subject Identifier | text     | 40   | Derived  | Identifier       | Req  | 003      |         |          |         | IN       |
| DM      | BRTHTC  | Date/Time of Birth        | datetime | 19   | CRF      | Record Qualifier | Perm | 016      |         |          | 44      | IN       |
| DM      | SEX     | Sex                       | text     | 1    | CRF      | Record Qualifier | Req  | 019      | SEX     |          | 44      | IN       |
| DM      | RACE    | Race                      | text     | 200  | CRF      | Record Qualifier | Exp  | 020      | RACE    |          | 44      | IN       |
| DM      | ETHNIC  | Ethnicity                 | text     | 200  | CRF      | Record Qualifier | Perm | 021      | ETHNIC  |          | 44      | IN       |

## THE KEY TO A COMPLETE DEFINE.XML

| DATASET | VARNAME | VARLABEL                  | DATATYPE | LENGTH | ORIGIN   | VALUE            |
|---------|---------|---------------------------|----------|--------|----------|------------------|
| DM      | STUDYID | Study Identifier          | text     | 40     | Protocol | Identifier       |
| DM      | DOMAIN  | Domain Abbreviation       | text     | 2      | Assigned | Identifier       |
| DM      | USUBJID | Unique Subject Identifier | text     | 40     | Derived  | Identifier       |
| DM      | BRTHDTC | Date/Time of Birth        | datetime | 19     | CRF      | Record Qualifier |
| DM      | SEX     | Sex                       | text     | 1      | CRF      | Record Qualifier |
| DM      | RACE    | Race                      | text     | 200    | CRF      | Record Qualifier |
| DM      | ETHNIC  | Ethnicity                 | text     | 200    | CRF      | Record Qualifier |

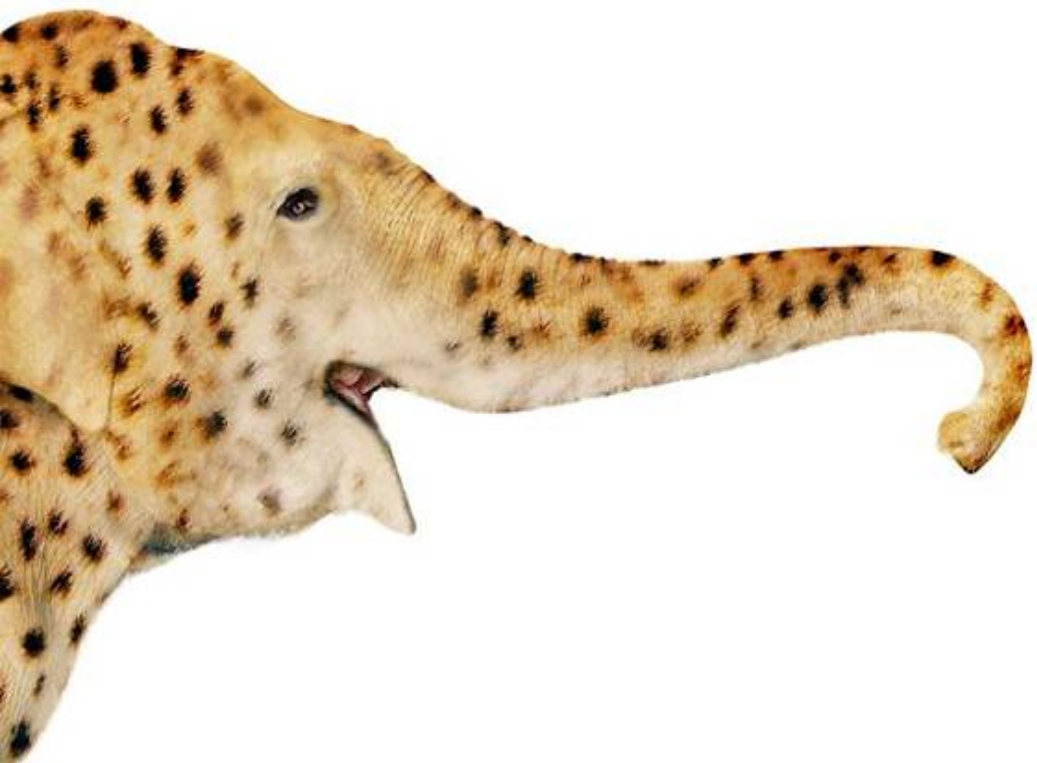
| VARROLE          | CORE | VARORDER | CODELST | VALUEOID | CRFPAGE | SGSSTATE |
|------------------|------|----------|---------|----------|---------|----------|
| Identifier       | Req  | 001      |         |          |         | IN       |
| Identifier       | Req  | 002      | DOMAIN  |          |         | IN       |
| Identifier       | Req  | 003      |         |          |         | IN       |
| Record Qualifier | Perm | 016      |         |          | 44      | IN       |
| Record Qualifier | Req  | 019      | SEX     |          | 44      | IN       |
| Record Qualifier | Exp  | 020      | RACE    |          | 44      | IN       |
| Record Qualifier | Perm | 021      | ETHNIC  |          | 44      | IN       |

## THE KEY TO A COMPLETE DEFINE.XML

- Living document
- External data
- Randomisation
- Blinded data
- Changes in SDTM implementation guide
- Length for character variables

## CONCLUSIONS

- In-house developed software tools
- Facilitate, speed up and improve quality
  - Annotation tool
  - SDTM Mapping tool
- Provide information needed to automatically create accurate metadata
- Future proof: easily integrate new standards in our different software tools
- Flexibility



# SGS

THANK YOU FOR YOUR ATTENTION

**CONTACT US**

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**WHERE EXPERIENCE  
MEETS SPEED**

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