Re-mastering the define-xml and its “brother” the Reviewer Guide

Presented by Angelo Tinazzi
Senior Director, Standards, Systems and CDISC Consulting - Statistical Programming
Cytel Inc. - angelo.tinazzi@cytel.com
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>20 Years of Experience
Passion for Standards
Member of CDISC-EU Committee
CDISC Authorized Instructor for ADaM
Agenda

1. Introduction
   • Quality in Data Submission
   • Intro to the Reviewer Guide and the define-xml
   • Initial (Final) Recommendations
   • Official and Unofficial References
2. (Unveiled?) Tips
3. Conclusions
Introduction

Quality in Data Submission
Intro to the Reviewer Guide and the define-xml
Initial (Final) Recommendations
Official and Unofficial References
Introduction

Quality in Data Submission

*What do we mean by “Quality”*

- Any “piece” submitted to HA should be of **Good Quality**
- Quality in the **Data**
- Quality in the **Results**
- (But also) Quality in the **Documentation**
  - define-xml
  - Reviewer Guide
  - aCRF
  - Any other “attached” submitted document, including scripts e.g. SAS code

“The efficacy and safety of your drug are of course what matter, but **lack of traceability, poor or insufficient documentation might trigger questions and concerns from the reviewer.** You may think these are minor issues because they do not ultimately impact any results. However, **you are risking your credibility with the FDA reviewer, who may conclude that your package is not of good quality**” A. Tinazzi “The CDISC Stupidario (the CDISC Nonsense)”, CDISC-EU 2019
Introduction

Intro to the Reviewer Guide and the define-xml

Regulatory Interaction
They facilitate the communication with the reviewer

Reviewer Guide
Single point of orientation, nsdrg (SEND) csdrg (SDTM) adrg (ADaM)

define-xml
Set of machine readable Metadata, required by FDA and PMDA for SEND, SDTM and ADaM, Platform Independent and Vendor Neutral
**Introduction**

**Initial (Final) Recommendations**

| Start with the « end » in Mind | • Do not wait the end to generate define-xml  
| • The reviewer guide is a working document, it could be your programming « notebook » |
| define-xml can drive Automation | • Make sure your metadata are accurate e.g. reference the correct Ig/CT versions |
| Clarity of Explanations | • Reduce the risk to have questions back from the reviewer because something is unclear |
| Establish Conventions | • Naming conventions for code-list, derivations and comments  
| • Standard wording for methods and comments |
| Review Process | • Make sure there is an internal review process, automatic and manual  
| • Be pragmatic and Use Common Sense  
| • Educate, there is “more” than the CDISC standards when it’s time to submit to HA |
Introduction

Intro to the Reviewer Guide and the define-xml

Official Standards
- define-xml 2.0 + Analysis Results Metadata (ARM) Specification 1.0
- define-xml 2.1 which includes ARM

Agency Recommended Templates
- PhUSE WG, Clinical Study Data Reviewer Guide Template and Guidance
- PhUSE WG, Analysis Data Reviewer Guide Template and Guidance

Good Recommendations
- PhUSE WG, “Define-xml Version 2.0 Completion Guidelines”
(Unveiled?) Tips

1. When do I need to create ValueLevel Metadata
2. When do I need to assign / specify a codelist?
3. Use of subset codelist
4. When origin=CRF and you have to link to Multiple Pages
5. Origin=Assigned vs Origin=Dervied
6. Reviewer Guide vs define-xml
7. SDTM Mapping Specifications are not needed in define-xml
8. Good vs Bad Computational Algorithms
9. Consistency between SDTM and ADaM define-xml
(Unveiled?) Tips

1. When do I need to create ValueLevel Metadata?
   - The SDTM /ADAM models are highly normalized data structures e.g. Findings for SDTM or BDS for ADaM.
   - As a result there are some cases where the content of a column or variable cannot be unambiguously defined through Variables Metadata.

Value Level Metadata - VS [VSORRES]

<table>
<thead>
<tr>
<th>Variable</th>
<th>Where</th>
<th>Type</th>
<th>Length / Display Format</th>
<th>Controlled Terms or Format</th>
<th>Origin</th>
<th>Derivation/Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>VSORRES</td>
<td>VTESTCD EQ DBP (Diastolic Blood Pressure)</td>
<td>integer</td>
<td>2</td>
<td></td>
<td>CRF Page 11</td>
<td></td>
</tr>
<tr>
<td>VSORRES</td>
<td>VTESTCD EQ SBP (Systolic Blood Pressure)</td>
<td>integer</td>
<td>3</td>
<td></td>
<td>CRF Page 11</td>
<td></td>
</tr>
<tr>
<td>VSORRES</td>
<td>VTESTCD EQ PULSE (Pulse Rate)</td>
<td>integer</td>
<td>2</td>
<td></td>
<td>CRF Page 11</td>
<td></td>
</tr>
<tr>
<td>VSORRES</td>
<td>VTESTCD EQ WEIGHT (Weight)</td>
<td>float</td>
<td>5.1</td>
<td></td>
<td>CRF Page 11</td>
<td></td>
</tr>
<tr>
<td>VSORRES</td>
<td>VTESTCD EQ HEIGHT (Height)</td>
<td>float</td>
<td>5.1</td>
<td></td>
<td>CRF Page 11</td>
<td></td>
</tr>
<tr>
<td>VSORRES</td>
<td>VTESTCD EQ FRMSIZE (Body Frame Size)</td>
<td>text</td>
<td>6</td>
<td>[<em>LARGE</em>, &quot;MEDIUM&quot;, &quot;SMALL&quot;] &lt;Size&gt;</td>
<td>CRF Page 11</td>
<td></td>
</tr>
</tbody>
</table>
(Unveiled?) Tips

1. When do I need to create ValueLevel Metadata?
   - All SDTM Supplemental Qualifiers √

<table>
<thead>
<tr>
<th>Variable</th>
<th>Where</th>
<th>Type</th>
<th>Length / Display Format</th>
<th>Controlled Terms or Format</th>
<th>Origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>QVAL</td>
<td>QNAM = &quot;APPETHIS&quot; (History of appetite suppressant use)</td>
<td>text</td>
<td>18</td>
<td>History of Appetite suppressant use</td>
<td>CRF Page 13</td>
</tr>
<tr>
<td>QVAL</td>
<td>QNAM = &quot;CATHLTYPE&quot; (Catheter Lumen Type)</td>
<td>text</td>
<td>12</td>
<td>[&quot;Double lumen&quot;, &quot;Double lumen&quot;, &quot;Single lumen&quot;, &quot;U&quot; = &quot;Unknown&quot;]</td>
<td>CRF Page 65</td>
</tr>
<tr>
<td>QVAL</td>
<td>QNAM = &quot;CATHTYPE&quot; (Catheter Type)</td>
<td>text</td>
<td>8</td>
<td>Catheter Type</td>
<td>CRF Page 65</td>
</tr>
<tr>
<td>QVAL</td>
<td>QNAM = &quot;CLOSEHUB&quot; (Patient Using Closed Hub System?)</td>
<td>text</td>
<td>1</td>
<td>[&quot;N&quot; = &quot;No&quot;, &quot;U&quot; = &quot;Unknown&quot;, &quot;Y&quot; = &quot;Yes&quot;]</td>
<td>CRF Page 65</td>
</tr>
<tr>
<td>QVAL</td>
<td>QNAM = &quot;CMACON&quot; (Medication Action)</td>
<td>text</td>
<td>11</td>
<td>[&quot;Change&quot;, &quot;Discontinue&quot;, &quot;Start&quot;]</td>
<td>CRF Page 63</td>
</tr>
</tbody>
</table>

- Trial Summary (TS) √
- All findings? √ √ Inclusion / Exclusion Criteria (IE)? √
- All ADaM BDS? √ √
(Unveiled?) Tips

1. When do I need to create ValueLevel Metadata (cont)
   - Is it really needed here?

Value Level Metadata - DM [ARMCD]

<table>
<thead>
<tr>
<th>Variable</th>
<th>Where</th>
<th>Type</th>
<th>Length / Display Format</th>
<th>Controlled Terms or Format</th>
<th>Origin</th>
<th>Derivation/Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARMCD</td>
<td>ARMCD = &quot;ENROLLED&quot; (Enrolled)</td>
<td>text</td>
<td>200</td>
<td></td>
<td>Assigned</td>
<td>Set to ENROLLED when patient is enrolled into the study (no screen failure, eligible for the study)</td>
</tr>
<tr>
<td>ARMCD</td>
<td>ARMCD = &quot;SCREENFAIL&quot; (Screen Failure)</td>
<td>text</td>
<td>200</td>
<td></td>
<td>Derived</td>
<td>Set to SCREENFAIL when reason for discontinuation is &quot;Protocol Deviation: Ineligible Patient&quot; or &quot;Duplicate data entry&quot;</td>
</tr>
</tbody>
</table>

Value Level Metadata - DM [RACE]

<table>
<thead>
<tr>
<th>Variable</th>
<th>Where</th>
<th>Type</th>
<th>Length / Display Format</th>
<th>Controlled Terms or Format</th>
<th>Origin</th>
<th>Derivation/Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>RACE</td>
<td>ETHNIC = &quot;HISPANIC OR LATINO&quot; (Hispanic or Latino)</td>
<td>text</td>
<td>200</td>
<td></td>
<td>Derived</td>
<td>RACE=OTHER IF ETHNIC = HISPANIC OR LATINO</td>
</tr>
<tr>
<td>RACE</td>
<td>ETHNIC = &quot;NULL&quot;</td>
<td>text</td>
<td>200</td>
<td></td>
<td>CRF Page 4</td>
<td></td>
</tr>
</tbody>
</table>

Value Level Metadata - DM [SEX]

<table>
<thead>
<tr>
<th>Variable</th>
<th>Where</th>
<th>Type</th>
<th>Length / Display Format</th>
<th>Controlled Terms or Format</th>
<th>Origin</th>
<th>Derivation/Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEX</td>
<td>SEX = &quot;F&quot; (Female)</td>
<td>text</td>
<td>200</td>
<td></td>
<td>CRF Page 4</td>
<td></td>
</tr>
<tr>
<td>SEX</td>
<td>SEX = &quot;M&quot; (Male)</td>
<td>text</td>
<td>200</td>
<td></td>
<td>CRF Page 4</td>
<td></td>
</tr>
<tr>
<td>SEX</td>
<td>SEX = &quot;U&quot; (Unknown)</td>
<td>text</td>
<td>200</td>
<td></td>
<td>Derived</td>
<td>Set to &quot;U&quot; when SEX is not reported in the CRF</td>
</tr>
</tbody>
</table>
(Unveiled?) Tips

2. When do I need to assign / specify a codelist?
- Whenever in the Ig a variable has a **CDISC-CT** associated
- SDTM variables with **pre-printed code-list** in the CRF
- In general variables or VLMs with a « **finite** » set of values e.g. it is not applicable to free-text
- **ADaM variables copied from SDTM** when the SDTM variables have a codelist defined (traceability)

Make use of subset-codelist
e.g. see example later for CM and LB Unit
→ **See tip nr. 3**
(Unveiled?) Tips

2. When do I need to assign / specify a codelist? (cont)

Numeric Variables with a decode or variables containing abbreviated text:

- VISITNUM with decode from VISIT
- QNAM with decode from QLABEL

VISITNUM Mapping

<table>
<thead>
<tr>
<th>Permitted Value (Code)</th>
<th>Display Value (Decode)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Enrollment</td>
</tr>
<tr>
<td>120</td>
<td>1 Year Interval</td>
</tr>
</tbody>
</table>

Qualifier Variable Name for Supplemental Qualifiers for MH

<table>
<thead>
<tr>
<th>Permitted Value (Code)</th>
<th>Display Value (Decode)</th>
</tr>
</thead>
<tbody>
<tr>
<td>APAHDIA1</td>
<td>Associated PAH Diagnosis 1</td>
</tr>
<tr>
<td>APAHDIAG</td>
<td>Associated PAH Diagnosis</td>
</tr>
<tr>
<td>APAHTYPE</td>
<td>Associated PAH Type</td>
</tr>
</tbody>
</table>

- --TESTCD with decode from --TEST
- PARAM PARAMN with decode from PARAM
- PARAMCD with decode from PARAM
(Unveiled?) Tips

2. When do I need to assign / specify a codelist? (cont)

The following do **NOT need a codelist** to be defined in define-xml

- MedDRA, WHO-DD, etc. → External Dictionaries
- ISO 8601 (date/time/duration) → External Standard format handled by the stylesheet
- ISO 3166 (country) → Yes recommended to create a codelist with “applicable” countries
(Unveiled?) Tips

3. Use of subset codelist

- CDISC-CT can be a “superset” of terms used across different variables, datasets e.g. UNIT

- Not all terms are applicable to all variables where the same CDISC-CT is used e.g. CMDOSU and LBORRESU

This unit very likely does not apply to Laboratory Tests
(Unveiled?) Tips

3. Use of subset codelist (cont)
- Do not create one UNIT CT for CMDOSU and LBORRESU
- Create **two separate unit codelists as a “subset” of the CDISC-CT UNIT**

<table>
<thead>
<tr>
<th>Permitted Value (Code)</th>
<th>Display Value (Decode)</th>
</tr>
</thead>
<tbody>
<tr>
<td>g/L [C42576]</td>
<td>Kilogram per Cubic Meter</td>
</tr>
<tr>
<td>mg/dL [C67015]</td>
<td>Milligram per Deciliter</td>
</tr>
<tr>
<td>mol/L [C48555]</td>
<td>Mole per Liter</td>
</tr>
<tr>
<td>pg/mL [*]</td>
<td>Picogram per Milliliter</td>
</tr>
<tr>
<td>umol/L [C48508]</td>
<td>Micromole per Liter</td>
</tr>
<tr>
<td>ng/L [C67327]</td>
<td>Nanogram per Liter</td>
</tr>
<tr>
<td>pmol/L [C67434]</td>
<td>Picomole per Liter</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Permitted Value (Code)</th>
<th>Display Value (Decode)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L/min [C67388]</td>
<td>L/min</td>
</tr>
<tr>
<td>OTHER [*]</td>
<td>Other</td>
</tr>
<tr>
<td>mL/min [C64777]</td>
<td>Milliliter per Minute</td>
</tr>
<tr>
<td>mL/min/m2 [*]</td>
<td>Milliliter per Minute per Square Meter</td>
</tr>
<tr>
<td>mg [C26253]</td>
<td>Milligram</td>
</tr>
<tr>
<td>mg/L [C64572]</td>
<td>mg/L</td>
</tr>
<tr>
<td>mg/h [C66969]</td>
<td>mg/h</td>
</tr>
</tbody>
</table>

**Units for Laboratory Results [CL.LBRESU, C71620]**

**Units for Concomitant Medications [CL.CMDOSU, C71620]**
(Unveiled?) Tips

4. When origin=CRF and you have to link to Multiple Pages
   - Make use of space and not comma

```xml
<def:PDFPageRef Type="NamedDestination" PageRefs="44, 45, 46, 47, 48"/>
```

These links to individual acrf pages will not work once the define-xml is rendered by the stylesheet.

```xml
<def:PDFPageRef Type="PhysicalRef" PageRefs="44 45 46 47 48"/>
```

These links to individual acrf pages will point to individual acrf pages once the define-xml is rendered by the stylesheet.
(Unveiled?) Tips

5. Origin=Assigned vs Origin=Derived

Derived
- “If the variable or set of parameter analysis values is calculated, then origin type is Derived”. **Variables derived in the eDC are not considered derived**

Assigned: From CDISC “Data that is determined by **individual judgment** (by an evaluator other than the subject or investigator)... This may include third party attributions by an adjudicator“ or “Values that are set independently of any subject-related data values in order to complete SDTM fields such as DOMAIN and --TESTCD are considered to have an origin type of ‘Assigned’”. Other examples

- **Secondary Variables** in ADaM e.g. SEXN (secondary of character SEX)
- **Logically Synonimous** e.g. PARAM/PARAMCD/PARAMN
(Unveiled?) Tips

6. Reviewer Guide vs define-xml - When it’s time to find alternatives to define-xml

<table>
<thead>
<tr>
<th>TRTA</th>
<th>Actual Treatment</th>
<th>text</th>
<th>14</th>
<th>TRT</th>
<th>Derived:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Set to &quot;SCREEN FAILURE&quot; for all screen failures (check if ADSL.ACTARM = &quot;SCREEN FAILURE&quot;) and set to &quot;NOT TREATED&quot; for all patients not treated (check if ADSL.ACTARM = &quot;NOT TREATED&quot;). For all other patients the following rules apply: If study is not in (&quot;E&quot;, &quot;F&quot;) then set to ADTREAT.TRTA. Else If study = &quot;E&quot; then do: If SR.EPOCH in(&quot;SCREENING&quot;, &quot;BLINDED TREATMENT&quot;) set to ADTREAT.TRTA where ADTREAT.APHASE = &quot;BLINDED TREATMENT&quot;, else if SR.EPOCH in(&quot;FOLLOW-UP&quot;, &quot;OPEN LABEL TREATMENT&quot;, &quot;OPEN LABEL TREATMENT EXT&quot;) set to ADTREAT.TRTA where ADTREAT.APHASE = &quot;OPEN LABEL TREATMENT&quot;, else if SR.EPOCH is missing and SR.SRDTC is not missing then do: if SR.SRDTC &lt;= ADTREAT.AENDT where ADTREAT.APHASE = &quot;BLINDED TREATMENT&quot; then set to ADTREAT.TRTA where ADTREAT.APHASE = &quot;BLINDED TREATMENT&quot;, else set to ADTREAT.TRTA where ADTREAT.APHASE = &quot;OPEN LABEL TREATMENT&quot;. Else if study = &quot;F&quot; then do: If SR.EPOCH in(&quot;SCREENING&quot;, &quot;OPEN LABEL FIRST TREATMENT&quot;) set to ADTREAT.TRTA where ADTREAT.APHASE = &quot;OPEN LABEL FIRST TREATMENT&quot;, else if SR.EPOCH in(&quot;FOLLOW-UP&quot;, &quot;OPEN LABEL SECOND TREATMENT&quot;) set to ADTREAT.TRTA where ADTREAT.APHASE = &quot;OPEN LABEL SECOND TREATMENT&quot;, else if SR.EPOCH is missing and SR.SRDTC is not missing then do: if SR.SRDTC &lt; ADTREAT.TRTSDT where ADTREAT.APHASE = &quot;OPEN LABEL SECOND TREATMENT&quot; then set to ADTREAT.TRTA where ADTREAT.APHASE = &quot;OPEN LABEL FIRST TREATMENT&quot; else set to ADTREAT.TRTA where ADTREAT.APHASE = &quot;OPEN LABEL SECOND TREATMENT&quot;</td>
</tr>
</tbody>
</table>
(Unveiled?) Tips

6. Reviewer Guide vs define-xml - When it’s time to find alternatives (cont)

- define.xml has some **visual limitations**
- Long text might be not always readable
- If you see your text could be not read, than it’s time to find an alternative to define.xml

<table>
<thead>
<tr>
<th>AVISIT</th>
<th>Analysis Visit</th>
<th>text</th>
<th>25</th>
<th>Derived:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>See SAP 4.8.5 for the time frames Calculate the time frames (AVISIT) checking whether the related SR.SRDT is in the frame of the period starting at Date of first exposure to treatment (ADSL.TRTSDT).</td>
</tr>
</tbody>
</table>

**AVISIT Derivation Algorithm**
(Unveiled?) Tips

7. SDTM Mapping Specifications are not needed in define-xml

<table>
<thead>
<tr>
<th>ARM</th>
<th>Description of Planned Arm</th>
<th>text</th>
<th>14</th>
<th>[&quot;Enrolled&quot;, &quot;Screen Failure&quot;]&lt;Arm&gt;</th>
<th>Assigned</th>
<th>Taken from IVRS dataset RANDOM.TRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTARMCD</td>
<td>Actual Arm Code</td>
<td>text</td>
<td>8</td>
<td>[&quot;ENROLLED&quot; = &quot;Enrolled&quot;, &quot;SCRNFAL&quot; = &quot;Screen Failure&quot;]&lt;Arm (Code)&gt;</td>
<td>Derived</td>
<td>Same as ARMCD</td>
</tr>
<tr>
<td>ACTARM</td>
<td>Description of Actual Arm</td>
<td>text</td>
<td>14</td>
<td>[&quot;Enrolled&quot;, &quot;Screen Failure&quot;]&lt;Arm&gt;</td>
<td>Assigned</td>
<td>Assigned from TA.ARM based on ACTARMCD.</td>
</tr>
<tr>
<td>COUNTRY</td>
<td>Country</td>
<td>text</td>
<td>3</td>
<td>ISO 3166</td>
<td>Assigned</td>
<td>Derived from SITEINFO.CTRY</td>
</tr>
</tbody>
</table>

- RANDOM.TRT what?
- SITEINFO.CTRY what?

These are mapping specifications and they should be not included in the define.xml!!!
(Unveiled?) Tips

8. Good vs Bad Computational Algorithms (Methods)
- Avoid use of programming code or “only” programming code e.g. SAS

<table>
<thead>
<tr>
<th>PCHG</th>
<th>Percent Change from Baseline</th>
<th>float</th>
<th>Analysis Parameter</th>
<th>12 Derived</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(((AVAL-BASE)*100)/BASE</td>
</tr>
</tbody>
</table>

This is acceptable and straightforward to understand
8. Good vs Bad Computational Algorithms (Methods) (cont)

- Avoid use of programming code or “only” programming code e.g. SAS

**Not Acceptable. “I miss the rationale!!!!”**

```plaintext
If PAANLFL = 'Y' then do;
  If SCRNOCFL ne 'Y' then APHASE = 'From Day 1 to Week 12';
  Else if SCRNOCFL ne 'Y' and PAANLFL ne 'Y' and FUPOCFL ne 'Y' then APHASE = 'From Week 12 to Week 24';
  End;
Else if EXTFL = "Y" then do;
  If ASTDT > W24VISDT and FUPOCFL ne 'Y' then APHASE = "From Week 24 to Week 52";
  Else if EXTFL ne 'Y' and FUPOCFL = 'Y' then APHASE = "From Week 24 to Week 48";
  End;
```

- What's the difference?
- Which subset of subjects is selected here?
- ....
8. Good vs Bad Computational Algorithms (Methods) (cont)
- Avoid “concise” description e.g. repeating what is already stated in the SAP

“Daily average rescue medication consumption as per information collected in the concomitant medications page.”
8. Good vs Bad Computational Algorithms (Methods) (cont)
- Avoid “concise” description e.g. repeating what is already stated in the SAP

“Daily average rescue medication consumption as per information collected in the concomitant medications page.

It is derived from CM.CMDOSTXT where CM.CMDECOD='Paracetamol'.
More details can be found in the Rescue Medications Consumption Derivation document”
(Unveiled?) Tips

9. Consistency between SDTM and ADaM define-xml

(Traceability in SDTM/ADaM Metadata)

**SDTM Only**: source variables and records not used in ADaM i.e. Screen Failures, IE domain, Suppl. Lab. Data, etc.

**SDTM and ADaM**: variables and records copied from SDTM to ADaM

**ADaM Only**: derived or assigned variables / new records in ADaM for analysis purpose

**Traceability Issue 1**
Check for ADaM Origin=Predecessor
- Keep all variables attributes from SDTM
- Bring codelist defined in SDTM
- Content must be not changed
The same applies when Predecessor is another ADaM

**Easy to check programmatically**

**Traceability Issue 2**
Check for Clear Pattern of Derivations
Creation of Records if needed
e.g. impute missing observations
Clear description of derivations

**It requires more Independent and Manual Review**
(Unveiled?) Tips

9. Consistency between SDTM and ADaM define-xml
(Traceability in SDTM/ADaM Metadata)

- Dataset Metadata e.g. Study Title
- Origin=Predecessor in ADaM
e.g. SUPPAE.QVAL where QNAM=AETRTEM for ADAE.AETRTEM
Conclusions
Conclusions

**Do not cut corners!** Try to imagine that you are the "recipient" of such package and check, for example, if the **explanation of a derivation in the define.xml is clear enough.**

Don’t get bored, **be patient, love and cure the standards!** Have a **passion for details** as they might matter when you submit your data to an agency. That’s what I try to pass on to my colleagues almost every day, the passion for the data especially when they are organized in a standard way.
References and Suggested Readings

- PhUSE WG, *Clinical Study Data Reviewer Guide and Analysis Data Reviewer Guide Template and Guidance*
- PhUSE WG, "*Best Practices for Documenting Dataset Metadata: Define-XML vs Reviewer's Guide*
- PhUSE WG, “*Define-xml Version 2.0 Completion Guidelines*”
- PhUSE WG, “*Metadata Definitions*”

- D. Roulstone, “*Do's and Don'ts of Define.xml*”, PhUSE-EU 2018, SA04
- S. Sirichenko, “*Diagnostic of technical errors in define-xml file*”, PhUSE-US 2018, SI07
- J. Schoeman, N. Perry, “*Define’ing the Future*”, PhUSE EU 2018, SI05
- S. Griffiths, “*ADaM Reviewer’s Guide – Interpretation and Implementation*”, PhUSE 2015, CD13
- M. Haloui and EL. Asam, “*High Quality Study Data Standards for Submission*”, PhUSE-US 2019, SA03
- V. Debbeti, “*How to Prepare High-quality Metadata for Submission*”, PhUSE-US 2018, SI12
- A. Tinazzi, “*The « CDISC Stupidario » (the CDISC Nonsense)*”, PhUSE-EU 2018, PP26
- A. Tinazzi, “*How to Ensure Quality in Data Submission*”, PharmaSUG-China 2019, DS-068
Thank You!
Backup slides
(Unveiled?) Tips

xx. Variable Metadata vs ValueLevel Metadata Consistency
- When a variable has only one Origin Type for all its values and it has VLM, three options:
  - Provide type only at variables metadata only, if all he same
  - Provide type only at VLM metadata only, if diff
  - Both but then the above hierarchy should be respected
Capture define-xml metadata in SAS

```sas
filename define "...\define.xml" ;
filename map "...\Work\defineXMLautomap.map";
libname define xmlv2 automap=replace xmlmap=MAP;
libname defineMt "...\Work";
proc copy inlib=define outlib=defineMt;
run;
libname define clear;
```

Accessing the Metadata from Define XML ", Lex Jansen, PharmaSUG 2018
(Unveiled?) Tips

xx. Clarity on Origin – define.xml v2.1

From “The Present and Future of Define-XML”, Lex Jansen, PhilaSUG 2018