PhUSE EU Connect 2018

SI05 Define’ing the Future

Nicola Perry and Johan Schoeman
• Difference’s in Define v2
• Consistency and Quality
• Hints and Tips
• Conclusion
Difference’s in Define v2
Difference’s in Define v2
Style Sheet Changes

Analysis Dataset Definitions

- New ‘Documentation’ column where the user can optionally include ADaM dataset level information, including links to ADRG.
- Dataset order follows dataset Class (SUBJECT LEVEL ANALYSIS DATASET, OCCURRENCE DATA STRUCTURE, BASIC DATA STRUCTURE, and ADAM OTHER and then alphabetically within Class).

<table>
<thead>
<tr>
<th>Dataset</th>
<th>Description</th>
<th>Class</th>
<th>Structure</th>
<th>Purpose</th>
<th>Keys</th>
<th>Location</th>
<th>Documentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADSL</td>
<td>Subject-Level Analysis</td>
<td>SUBJECT LEVEL ANALYSIS DATASET</td>
<td>One record per subject</td>
<td>Analysis</td>
<td>USUBJID, STUDYID</td>
<td>adsl.xpt</td>
<td>Includes screen failures</td>
</tr>
</tbody>
</table>
Difference’s in Define v2

Style Sheet Changes

Analysis Dataset Variable Definitions
- ‘Length/Display Format’ column.
- ‘Comment’ column changed to ‘Source/Derivation/Comment’.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Label</th>
<th>Type</th>
<th>Length / Display Format</th>
<th>Controlled Terms or Format</th>
<th>Source/Derivation/Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>STUDYID</td>
<td>Study Identifier</td>
<td>text</td>
<td>12</td>
<td></td>
<td>Predecessor: DM.STUDYID</td>
</tr>
<tr>
<td>USUBJID</td>
<td>Unique Subject Identifier</td>
<td>text</td>
<td>11</td>
<td></td>
<td>Predecessor: DM.USUBJID</td>
</tr>
<tr>
<td>SUBJID</td>
<td>Subject Identifier for the Study</td>
<td>text</td>
<td>4</td>
<td></td>
<td>Predecessor: DM.SUBJID</td>
</tr>
<tr>
<td>SITEID</td>
<td>Study Site Identifier</td>
<td>text</td>
<td>3</td>
<td></td>
<td>Predecessor: DM.SITEID</td>
</tr>
<tr>
<td>SITEGR1</td>
<td>Pooled Site Group 1</td>
<td>text</td>
<td>3</td>
<td></td>
<td>Derived: refer to SAP, Section 7.1 - if not pooled then SITEGR1=SITEID. If pooled, SITEGR1 will be 900</td>
</tr>
</tbody>
</table>
## Difference’s in Define v2

### Style Sheet Changes

### Value Level Metadata (VLM)

### Parameter Value List - ADTTE [AVAL]

<table>
<thead>
<tr>
<th>Variable</th>
<th>Where</th>
<th>Type</th>
<th>Length or Display Format</th>
<th>Controlled Terms or Format</th>
<th>Source / Derivation / Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVAL</td>
<td>PARAMCD = &quot;IPDISC&quot; (Study Treatment Discontinuation (days))</td>
<td>integer</td>
<td>8</td>
<td>[AVAL] = ADT - STARTDT + 1</td>
<td></td>
</tr>
</tbody>
</table>

### Parameter Value List - ADALSAQ [AVAL]

<table>
<thead>
<tr>
<th>Variable</th>
<th>Where</th>
<th>Type</th>
<th>Length or Display Format</th>
<th>Controlled Terms or Format</th>
<th>Source / Derivation / Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVAL</td>
<td>PARAMCD IN ( &quot;ALSA01&quot; (I have found it difficult to walk short distances, e.g. around the house.), &quot;ALSA02&quot; (I have fallen over whilst walking.), &quot;ALSA03&quot; (I have stumbled or tripped whilst walking.), &quot;ALSA04&quot; (I have lost my balance whilst walking.), &quot;ALSA05&quot; (I have had to concentrate whilst walking.))</td>
<td>integer</td>
<td>8</td>
<td>ALSA001 [6 Terms]</td>
<td>PREDECESSOR: QS.QSSTRESN WHERE QSTESTCD EQ PARAMCD</td>
</tr>
</tbody>
</table>
### Difference's in Define v2

#### Style Sheet Changes

**Controlled Terminology**

- Where Codes and Decodes are identical the terminology is only displayed once under ‘Permitted Value (Code)’.
- NCI codes are displayed, where applicable.

---

<table>
<thead>
<tr>
<th>APERIOD. [CL.APERIOD.]</th>
<th>DTYPE. [CL.DTYPE., C81224]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Permitted Value (Code)</strong></td>
<td><strong>Display Value (Decode)</strong></td>
</tr>
<tr>
<td>1</td>
<td>Treatment Period 1</td>
</tr>
<tr>
<td>2</td>
<td>Treatment Period 2</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**APERIODC. [CL.APERIODC.]**

<table>
<thead>
<tr>
<th>Permitted Value (Code)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Period 1</td>
</tr>
<tr>
<td>Treatment Period 2</td>
</tr>
</tbody>
</table>

* Extended Value
Difference’s in Define v2

Style Sheet Changes

Computational Algorithms

• Replaced with Computational Method element in Define v2.
• Required for all items with Origin=‘Derived’ and presented in the variable/value level metadata section.
• Summary of all algorithms/derivations for items entered with Origin=‘Derived’ included under ‘Analysis Derivations’
• Summary of all comments for items entered with Origin=‘Assigned’ included under ‘Comments’.

Analysis Derivations

<table>
<thead>
<tr>
<th>Method</th>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>MT.ADAE.ADURC</td>
<td>Computation</td>
<td>ADURN converted to display in days, hours and minutes</td>
</tr>
</tbody>
</table>

Comments

<table>
<thead>
<tr>
<th>CommentOID</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>COM.ADAE.AEOUTN</td>
<td>Numeric version of AEOUT</td>
</tr>
</tbody>
</table>
Difference’s in Define v2

Style Sheet Changes

Analysis Results Metadata (ARM)

- For Define v2 ARM is incorporated as part of the document

**Analysis Results Metadata - Detail**

<table>
<thead>
<tr>
<th>Display</th>
<th>Figure - 7.1 Kaplan Meier Survival Curves for Relapse-Free Efficacy over 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysis Result</td>
<td>Visual Comparisons between CQ Only, TQ + CQ and PQ + CQ.</td>
</tr>
<tr>
<td>Analysis Parameter(s)</td>
<td>PARAMCD = “RFE6M” (Relapse-free efficacy at six months)</td>
</tr>
<tr>
<td>Analysis Variable(s)</td>
<td>AVAI (Analysis Value)</td>
</tr>
<tr>
<td>Analysis Reason</td>
<td>Plot for primary/secondary assessment</td>
</tr>
<tr>
<td>Analysis Purpose</td>
<td>Plot for primary/secondary assessment</td>
</tr>
<tr>
<td>Data References (incl. Selection Criteria)</td>
<td>ADITTE1 [PARAMCD = “RFE6M” and CNSR IN (0, 1, 2, 3, 4, 5) and MITTEL = “V”]</td>
</tr>
<tr>
<td>Documentation</td>
<td>RAP section 11.1 Kaplan Meier Product Limit Estimates for mITT population.</td>
</tr>
<tr>
<td>Programming Statements</td>
<td>[SAS version 9.4]</td>
</tr>
<tr>
<td></td>
<td>Proc LIFETEST to generate Kaplan Meier Survival Estimates and Numbers at Risk. Plotted using PROC TEMPLATE and SGRENDER.</td>
</tr>
</tbody>
</table>
What are the new requirements?

- Three values for ADaM: PREDECESSOR, DERIVED and ASSIGNED.
- Null if VLM used (Origin part of VLM).
- Origin value appears as part of the text in the ‘Source/Derivation/Comment’ column in the Analysis Datasets variable metadata.

How do we implement?

- Our in-house documentation provides guidance on how to choose the most appropriate Origin value.
- Our in-house software, designed for setting up ADaM dataset metadata, has a field specifically for Origin and to assign a VLM name.
Difference’s in Define v2
Controlled Terminology

What are the new requirements?
• NCI codes should be included if appropriate.
• Extended values should be highlighted.

How do we implement?
• Our in-house software has been updated to include fields for entering NCI codes and for checking extended values.
• Our in-house standard ADaM metadata has been updated to include NCI codes.
Difference’s in Define v2
Value Level Metadata (VLM)

What are the new requirements?

• Define v2 has a ‘Where’ column.
• Parameter values can be included in one row.
• Origin needs to be defined for each row in the VLM.
• System independent operators must be used, for example, EQ, IN, NE.
• Can use AND in your where statements to narrow down the selection for your VLM definition (e.g. ADLB.PARAMCD EQ “HGB” and ADSL.SEX EQ “FEMALE”).

How do we implement?

• Our in-house software has been updated to accept a ‘Where’ clause and to add a field specifically for Origin. It also links with the controlled terminology for variables specified in the ‘Where’ column, such as PARAMCD, and adds the decode.
Difference’s in Define v2
Analysis Results Metadata (ARM)

What are the new requirements?
• ARM data to be incorporated into Define.xml document.

How do we implement?
• Our in-house software has been modified to allow easy entry of the information required to display ARM data in the Define.xml document.
Difference’s in Define v2
Impacts to the Analysis Data Reviewer’s Guide (ADRG)

Movement of Computational Algorithms section means lengthy and/or complex derivations are displayed at the variable level in the Analysis Datasets section.

ADRG utilised to explain lengthy and/or complex derivations:
• Included as part of Analysis Dataset description in ADRG Section 5.2.x
• Included as an Appendix (Section 8).
CONSISTENCY AND QUALITY
Consistency and Quality

How do we try and ensure consistency and quality in studies?

Causes of inconsistency and low quality:
- Multiple programmers
- Multiple reviewers
- Change of study team members during a study
- Lack of adherence to in-house standards
- Lack of adherence to CDISC standards
- Lack of training
- Aggressive timelines
Consistency and Quality

Methods to improve quality and consistency:

• Standard Metadata for all common ADaM domains updated to include NCI codes for controlled terminology and Origin.

• Review of eCRT package by experienced independent programmer.

• Training courses developed specific to Define.xml v2 production and eCRT package development.

• In-house system has built in error checking.

• Mandatory to run Pinnacle 21 on ADaMs (AD-- P21 IDs) and Define.xml only (DD-- P21 IDs).

• Focus on quality over time.
HINTS AND TIPS
Hints and Tips

• Start with the metadata for CRT package early in your study.
• Work on ADRG alongside Define to ensure that information is consistent.
• Get eCRT package reviewed by experienced independent programmer.
• Rerun and check the Pinnacle21 report through the course of the study on both SDTM and ADaM datasets.
• Definition of ORIGIN can be very programmer dependent. Create or update standard ADaM metadata to include an ORIGIN value to improve consistency. Here’s our take on defining ORIGIN…
Hints and Tips
Defining ORIGIN
Hints and Tips

Defining ORIGIN

ORIGIN=PREDECESSOR
Hints and Tips
Defining ORIGIN

ORIGIN=ASSIGNED
Hints and Tips

Defining ORIGIN

ORIGIN=DERIVED
Conclusion

- Major update requiring multiple modifications
- Major updates to software and documentation/standards
- Additional in-house training requirement
Define’ing the Future
Any Questions?