

PhUSE EU Connect 2018

SI05
Define'ing the Future

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- 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).

Dataset	Description	Class	Structure	Purpose	Keys	Location	Documentation
ADSL	Subject-Level Analysis	SUBJECT LEVEL ANALYSIS DATASET	One record per subject	Analysis	USUBJID, STUDYID	adsl.xpt	Includes screen failures

Difference's in Define v2

Style Sheet Changes



Analysis Dataset Variable Definitions

- 'Length/Display Format' column.
- 'Comment' column changed to 'Source/Derivation/Comment'.

Variable	Label	Type	Length / Display Format	Controlled Terms or Format	Source/Derivation/Comment
STUDYID	Study Identifier	text	12		Predecessor: DM.STUDYID
USUBJID	Unique Subject Identifier	text	11		Predecessor: DM.USUBJID
SUBJID	Subject Identifier for the Study	text	4		Predecessor: DM.SUBJID
SITEID	Study Site Identifier	text	3		Predecessor: DM.SITEID
SITEGR1	Pooled Site Group 1	text	3		Derived: refer to SAP, Section 7.1 - if not pooled then SITEGR1=SITEID. If pooled, SITEGR1 will be 900

Difference's in Define v2

Style Sheet Changes



Value Level Metadata (VLM)

- New layout with columns for 'Variable', 'Where', 'Type', 'Length or Display Format', 'Controlled Terms or Format' and 'Source/Derivation/Comment'.

Parameter Value List - ADTTE [AVAL]

Variable	Where	Type	Length or Display Format	Controlled Terms or Format	Source / Derivation / Comment
AVAL	PARAMCD = "IPDISC" (Study Treatment Discontinuation (days))	integer	8		Derived: AVAL=ADT - STARTDT + 1

Parameter Value List - ADALSAQ [AVAL]

Variable	Where	Type	Length or Display Format	Controlled Terms or Format	Source / Derivation / Comment
AVAL	PARAMCD IN ("ALSA01" (I have found it difficult to walk short distances, e.g. around the house.) , "ALSA02" (I have fallen over whilst walking.) , "ALSA03" (I have stumbled or tripped whilst walking.) , "ALSA04" (I have lost my balance whilst walking.) , "ALSA05" (I have had to concentrate whilst walking.))	integer	8	ALSAQ01 [6 Terms]	PREDECESSOR: QS.QSSTRESN WHERE QSTESTCD EQ PARAMCD

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.

APERIOD. [CL.APERIOD.]

APERIOD.

Permitted Value (Code)	Display Value (Decode)
1	Treatment Period 1
2	Treatment Period 2

APERIODC. [CL.APERIODC.]

APERIODC.

Permitted Value (Code)
Treatment Period 1
Treatment Period 2

DTYPE. [CL.DTYPE., C81224]

DTYPE.

Permitted Value (Code)	Display Value (Decode)
AVERAGE [C81209]	Average of Value Derivation Technique
IMPUTED [*]	Imputed from character value
LVPD [C132342]	Last Value Prior to Dosing Imputation Technique
WOCF [C81199]	Worst Observation Carried Forward Imputation Technique

* 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

Method	Type	Description
MT.ADAE.ADURC	Computation	ADURN converted to display in days, hours and minutes

Comments

CommentOID	Description
COM.ADAE.AEOUTN	Numeric version of AEOUT

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

Figure - 7.1

Display	Figure - 7.1 Kaplan Meier Survival Curves for Relapse-Free Efficacy over 6 months
Analysis Result	Visual Comparisons between CQ Only, TQ+CQ and PQ + CQ.
Analysis Parameter(s)	PARAMCD = "RFE6M" (Relapse-free efficacy at six months)
Analysis Variable(s)	AVAL (Analysis Value)
Analysis Reason	Plot for primary/secondary assessment
Analysis Purpose	Plot for primary/secondary assessment
Data References (incl. Selection Criteria)	ADTTE1 [PARAMCD = "RFE6M" and CNSR IN (0, 1, 2, 3, 4, 5) and MITTEL = "Y"]
Documentation	RAP section 11.1 Kaplan Meier Product Limit Estimates for mITT population.
Programming Statements	[SAS version 9.4] Proc LIFETEST to generate Kaplan Meier Survival Estimates and Numbers at Risk. Plotted using PROC TEMPLATE and SGRENDER.

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.

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**

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.



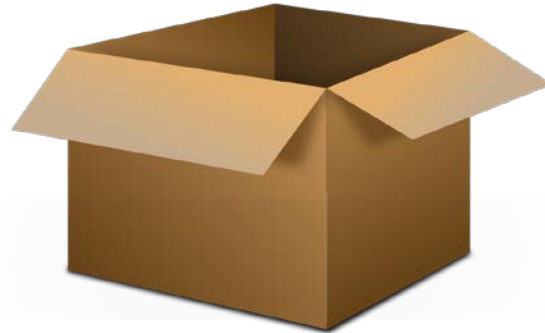
HINTS AND TIPS

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...

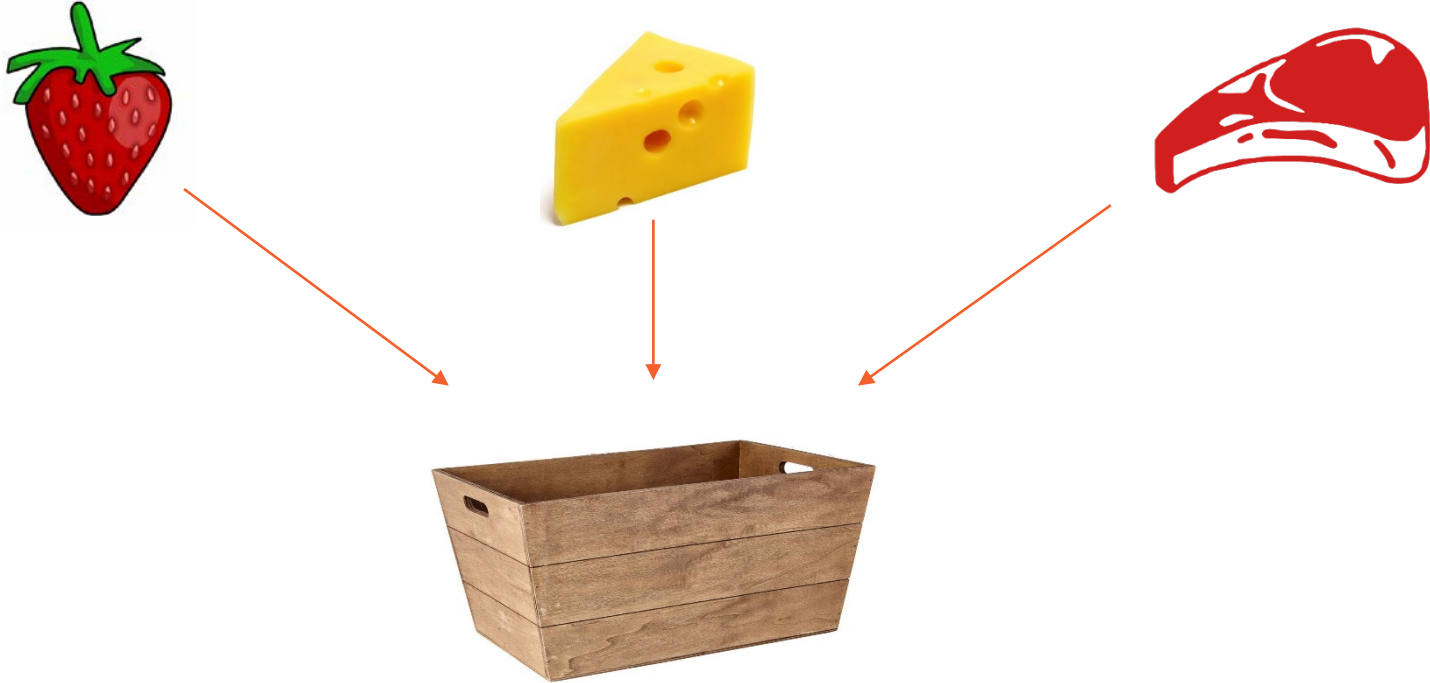
Hints and Tips

Defining ORIGIN



Hints and Tips

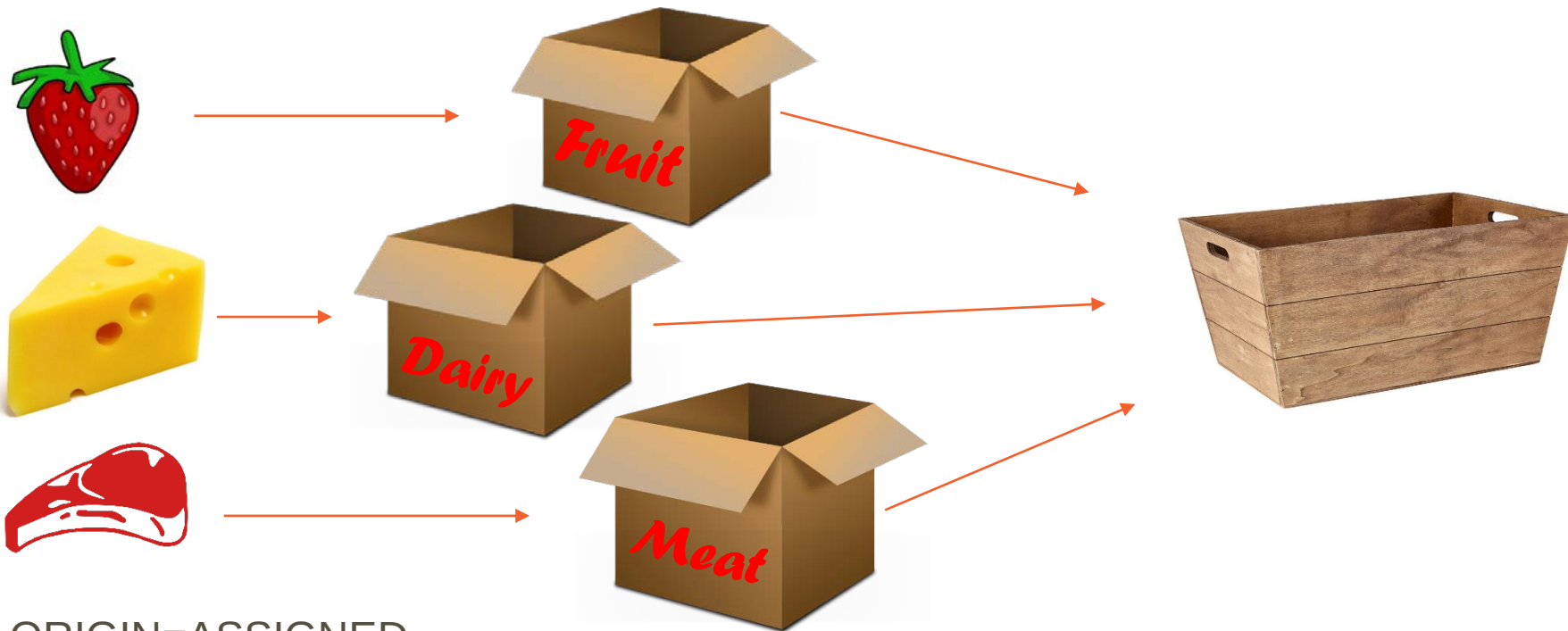
Defining ORIGIN



ORIGIN=PREDECESSOR

Hints and Tips

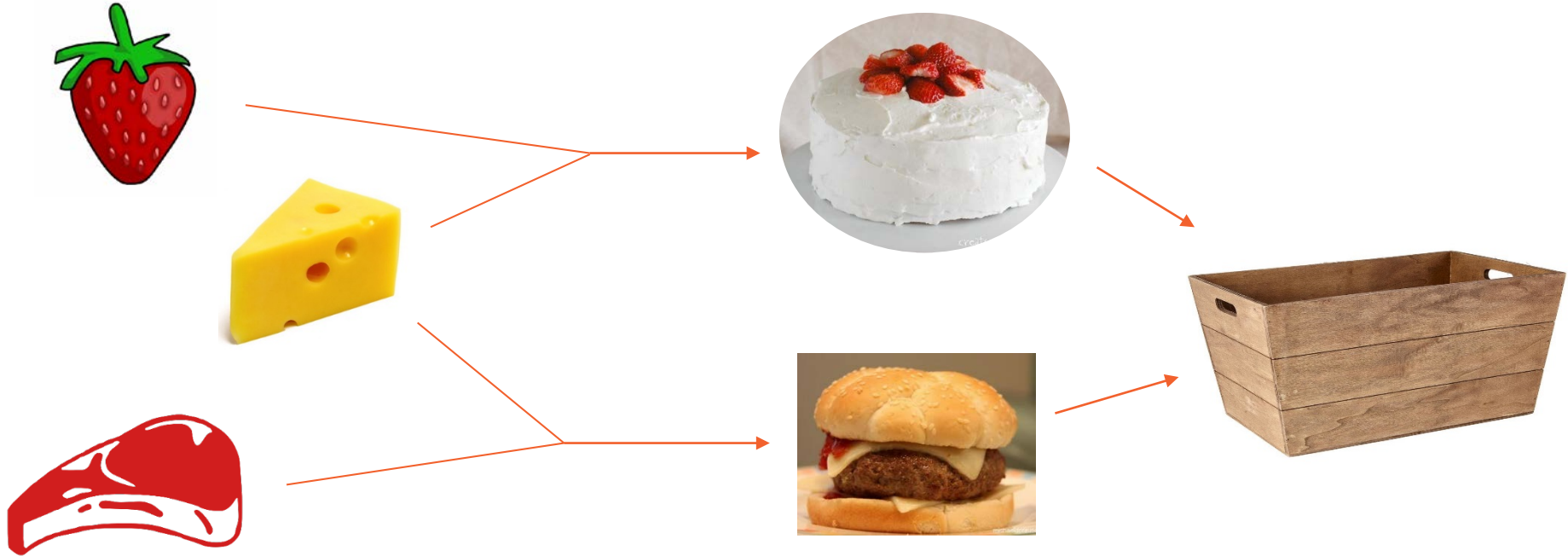
Defining ORIGIN



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?

