

CDISC Standards in Reverse: A More Efficient Approach to Clinical Trials Design

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Tables First

Tables are designed at the time of study and protocol development. The tables inform all aspects of database design and creation.

Tables inform analysis metadata

Table level metadata are filtered through ADaM and internal standard metadata libraries to pre-populate study level analysis metadata.

Tables inform SDTM metadata

Analysis metadata, which contains table level metadata, are filtered through SDTM standard metadata libraries to pre-populate study level SDTM metadata.

Tables inform data collection

Table metadata are used to pre-populate clinical database metadata and CRF panels.

TLP Library Mock Tables 3/7/2012

Table PE_TXB_01
Shift in Physical Examination Findings from Baseline to End of Study by Treatment Group

Parameter	Visit	Treatment A		Treatment B		Treatment C		Treatment D	
		Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal
HEENT	Baseline	100	0	100	0	100	0	100	0
	End of Study	100	0	100	0	100	0	100	0
MUSC	Baseline	100	0	100	0	100	0	100	0
	End of Study	100	0	100	0	100	0	100	0
SKIN	Baseline	100	0	100	0	100	0	100	0
	End of Study	100	0	100	0	100	0	100	0

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	End of Study	100	0	100	0	100	0	100	0
MUSC	Baseline	100	0	100	0	100	0	100	0
	End of Study	100	0	100	0	100	0	100	0
SKIN	Baseline	100	0	100	0	100	0	100	0
	End of Study	100	0	100	0	100	0	100	0

Table PE_TXB_01
Shift in Physical Examination Findings from Baseline to End of Study by Treatment Group

Display ID	Display Type	Display Identifier	Display Title	Select
60	Table	AE_TXB_02	Number and Percentage of Subjects with Most-Common Adverse Events by Treatment Group, System Organ Class, Preferred Term, and [Subgroup] - (Incidence Preferred Term >= X%)	No
61	Table	PE_TXA_01	Summary of Physical Examination Findings by Treatment Group and Visit	Yes
62	Table	PE_TXB_01	Shift in Physical Examination Findings from Baseline to End of Study by Treatment Group	No
63	Table	PE_TXB_01	Shift in Physical Examination Findings from Baseline to End of Study by Treatment Group	Yes
64	Table	PE_TXB_02	Shift in Physical Examination Findings from Baseline to End of Study by Treatment Group	No

DatasetName	Name	Label	Programming Definition	Type	Length	Code List
ADPE	PARAM	Parameter		C		
ADPE	AVAL	Analysis Value		N		
ADPE	AVALC	Analysis Value (C)		C		
ADPE	BASE	Baseline Value		C		
ADPE	SHIFTN	Shift1 (N)		N		

CDISC Analysis Data Model Version 2.1

Analysis Data Model (ADaM)

DatasetName	Name	Label	Programming Definition	Type	Length	Code List
ADPE	PARAM	Parameter	=PE.PETEST	C		18 Abdomen Cardiovascular General Appearance HEENT Musculoskeletal Neurological Other Respiratory Skin
ADPE	AVAL	Analysis Value	=1 if AVALC="NORMAL" =2 if AVALC="ABNORMAL"	N		8 1=NORMAL 2=ABNORMAL
ADPE	AVALC	Analysis Value (C)	=PE.PESTRESC	C		8 NORMAL ABNORMAL
ADPE	BASE	Baseline Value	=AVAL on record where ABLFL="Y" merged onto records by USUBJID PARAMCD	C		18 Baseline, Day 7, Day 28, Day 35
ADPE	SHIFTN	Shift1 (N)	=1 if ADPE.SHIFT1="ABNORMAL-ABNORMAL" =2 if ADPE.SHIFT1="ABNORMAL-NORMAL" =3 if ADPE.SHIFT1="NORMAL-ABNORMAL" =4 if ADPE.SHIFT1="NORMAL-NORMAL"	N		8 1=ABNORMAL-ABNORMAL, 2=ABNORMAL-NORMAL, 3=NORMAL-ABNORMAL, 4=NORMAL-NORMAL

Domain	varname	Label	ODMType	Core	Type	Length	Origin	Role	CT	ProgDef
PE	PETESTCD	Body System Examined Short Name	text	Req	Char			Topic		
PE	PETEST	Body System Examined	text	Req	Char			Synonym Qualifier		
PE	PEORRES	Verbatim Examination Finding	text	Exp	Char			Result Qualifier		
PE	PESTRSC	Character Result/Finding in Std Format	text	Exp	Char			Result Qualifier		

Domain	varname	Label	ODMType	Core	Type	Length	Origin	Role	CT	ProgDef
PE	PETESTCD	Body System Examined Short Name	text	Req	Char			Assigned Topic		Map PETESTCD from PETEST as follows: ABDOM-ABDOMEN CARDIO-CARDIOVASCULAR GENAPP-GENERAL APPEARANCE HEENT-HEENT MUSC-MUSCULOSKELETAL NEURO-NEUROLOGICAL OTHER-OTHER RESP-RESPIRATORY SKIN-SKIN
PE	PETEST	Body System Examined	text	Req	Char			18 CRF		ABDOMEN, CARDIOVASCULAR, GENERAL APPEARANCE, HEENT, MUSCULOSKELETAL, NEUROLOGICAL, OTHER, RESPIRATORY, SKIN
PE	PEORRES	Verbatim Examination Finding	text	Exp	Char			200 CRF		=pe(RAW.PE.PESTAT, NORMABN) if PEORRES="ABNORMAL", then append RAW.PE.PEORRES, separated by colon-space.
PE	PESTRSC	Character Result/Finding in Std Format	text	Exp	Char			200 Derived		=ABNORMAL if PEORRES starts with "ABNORMAL" =PEORRES otherwise

PHYSICAL EXAM DOMAIN=PE

Category	Result	If Abnormal, specify
General Appearance	☐ Normal ☐ Abnormal	PEORRES
Abdomen	☐ Normal ☐ Abnormal	
Skin	☐ Normal ☐ Abnormal	
Respiratory	☐ Normal ☐ Abnormal	

TLP Library Mock Tables 3/7/2012

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	End of Study	100	0	100	0	100	0	100	0
MUSC	Baseline	100	0	100	0	100	0	100	0
	End of Study	100	0	100	0	100	0	100	0
SKIN	Baseline	100	0	100	0	100	0	100	0
	End of Study	100	0	100	0	100	0	100	0

TLP Library Mock Tables 3/7/2012

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SKIN	Baseline	100	0	100	0	100	0	100	0
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MUSC	Baseline	100	0	100	0	100	0	100	0
	End of Study	100	0	100	0	100	0	100	0
SKIN	Baseline	100	0	100	0	100	0	100	0
	End of Study	100	0	100	0	100	0	100	0

DatasetName	Name	Label	Programming Definition	Type	Length	Code List
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ADPE	AVALC	Analysis Value (C)	=PE.PESTRESC	C		
ADPE	BASE	Baseline Value	=AVAL on record where ABLFL="Y" merged onto records by USUBJID PARAMCD	C		
ADPE	SHIFTN	Shift1 (N)		N		

Rho Metadata Editor

- ☐ Dataset Specifications
- ☐ Variable Definitions
- ☐ Crosswalks
- ☐ Import from Repository
- ☐ Select Another Study
- ☐ Close

Table, Listing, and Figure Library

Internal library of displays contains shells that are annotated for ADaM and are linked to metadata, programs, and documentation.

Mock displays to include in the final CSR are chosen at the time of protocol development.

Display Library

The selections made within the display library will not only inform the table, but also inform the ADaM metadata, the SDTM dataset metadata, the clinical datasets, and the CRF panels. Along with study-independent standards, this is the source of most of the metadata used in a study.

ADaM Metadata and Internal Metadata Library

Information from the table metadata libraries is filtered through two other sources: the ADaM standard and an internal metadata library. This creates a foundation more complete and reliable than starting from scratch or copying metadata from an unrelated study.

Study Level Analysis Dataset Metadata

The three sources of metadata (ADaM, internal library, table metadata) are combined to create the ADaM dataset metadata. Often these three sources are all that is needed, but if not, the amount of original thought will be minimal and restricted to places where thinking is desirable.

SDTM Metadata

Similar to the previous steps, metadata from the ADaM datasets are filtered through SDTM standards. Metadata from the SDTM standard are robust and does not require a separate internal library.

Study Level SDTM Metadata

The ADaM dataset metadata (a combination of ADaM, internal library, and table metadata) is combined with SDTM to create the study level SDTM dataset metadata. This combination leaves little to be defined on a custom basis.

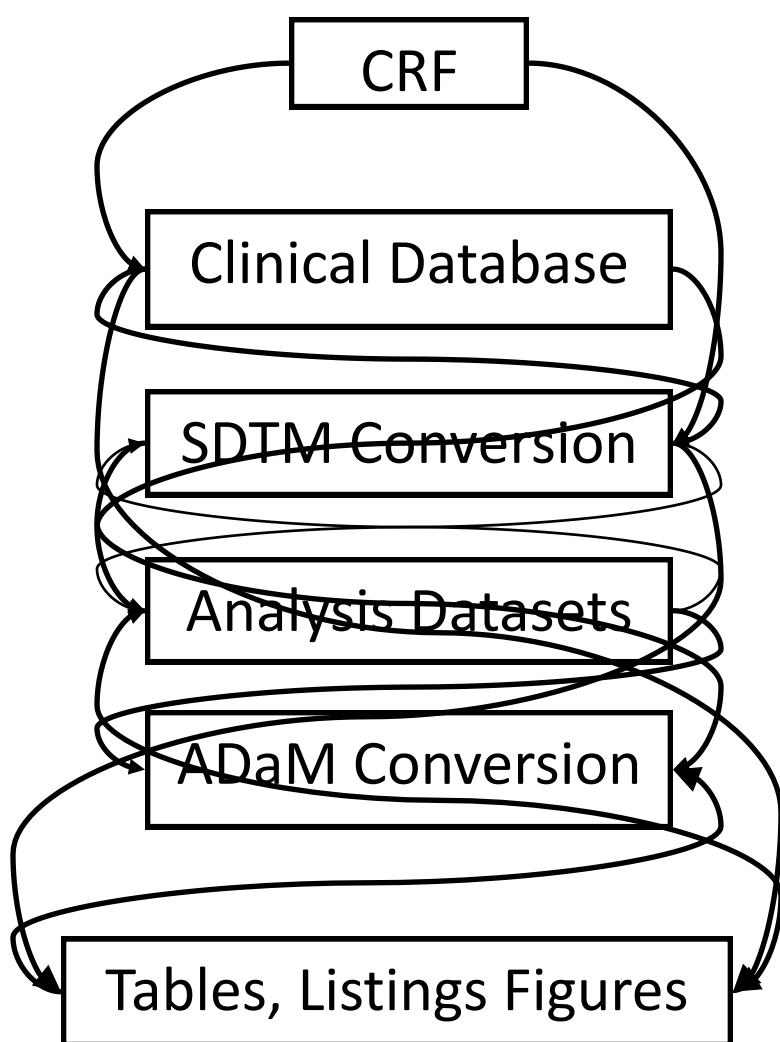
Summary

The FDA's acceptance of CDISC's SDTM and ADaM models has contributed to the increased use of CDISC standards in clinical trials. The use of standards and metadata for analysis reporting lags behind that of database production. Extending the end to end concept to analysis reporting can not only facilitate display production, but can also improve efficiency throughout the life cycle of a clinical trial. A tables-first approach produces more targeted CRF design and data collection; more efficient database and display creation; and improved quality based on the elimination of redundant processes.

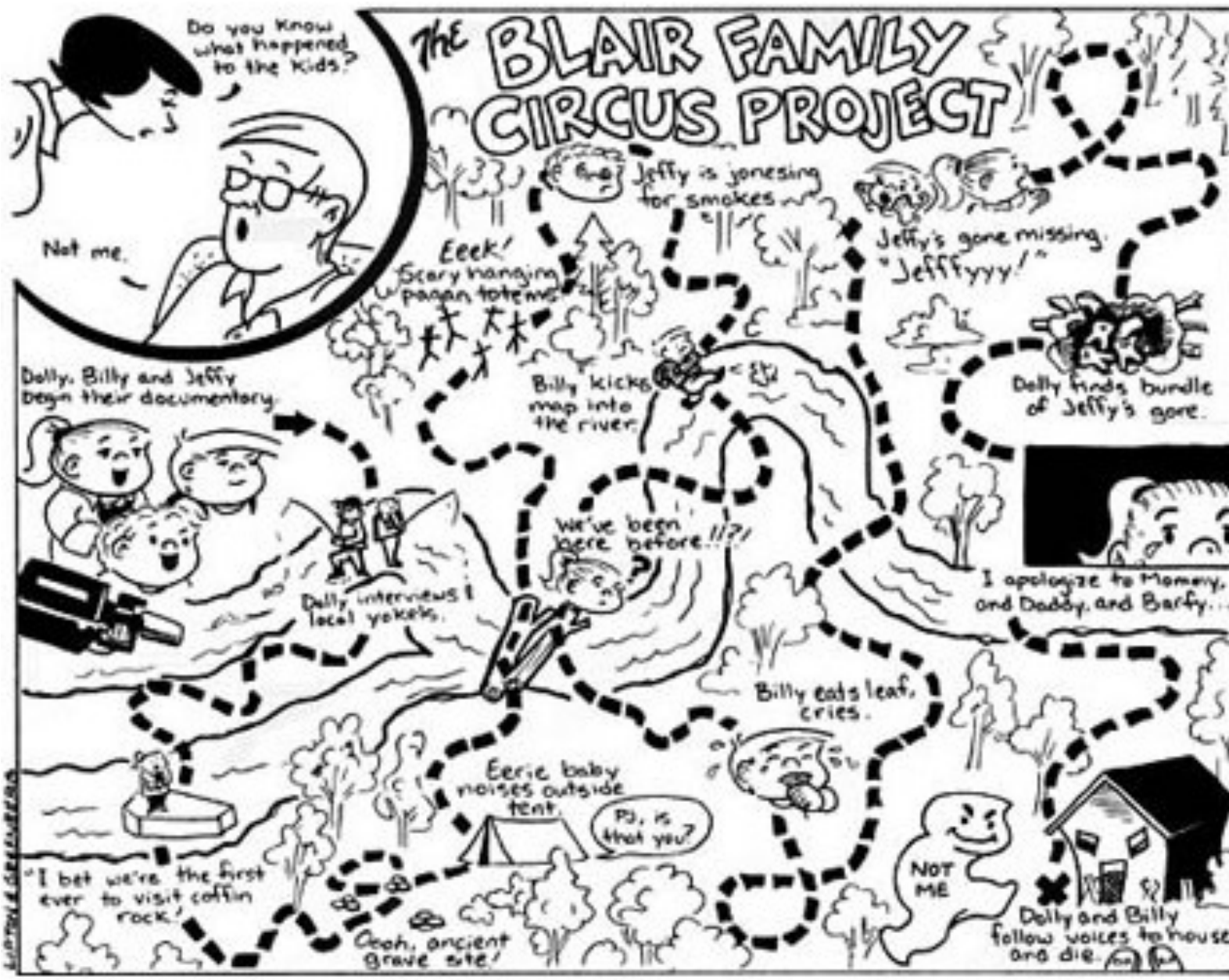
The Tables First Approach

- Each study has a purpose in a drug development program
- All required displays should be known prior to study start-up
- Use what is needed in tables to drive database design
- Standard ADaM/SDTM metadata facilitates a tables first approach

The Tables Last Approach (... aka how things are sometimes done today ...)



... or shown another way ...



The Display Library is linked to four metadata libraries: Treatments, Visits, Parameters, and Variables. The selections made within these libraries will not only inform the table, but also inform the ADaM metadata, the SDTM dataset metadata, the clinical datasets, and the CRF panels. Note: The information in these libraries is known before study start-up.

Parameter and Outcome Metadata Library. This library is populated from a repository of study parameters and outcomes. Parameters of interest for the display and expected outcomes are selected.

Parameter ID	Parameter	Parameter Abbreviation	Parameter Number	Finite Response	Finite Response (N)	Select
1	Abdomen	ABDOM	1	A/N	2,1	Yes
2	Chest/Lungs	CHEST	2	A/N	2,1	No
3	Extremities	EXT	3	NA		No
4	General Appearance	GENAPP	4	A/N	2,1	Yes
5	Heart	HEART	5	NA		No
6	HEENT	HEENT	6	A/N	2,1	Yes
7	Lymph Nodes	LYMPH	7	NA		No
8	Musculoskeletal	MUSC	8	A/N	2,1	Yes
9	Neck/Thyroid	NT	9	NA		No
10	Other	OTHER	10	A/N	2,1	Yes
11	Pulse	PULSE	11	NA		No
12	Respiratory	RESP	12	A/N	2,1	Yes
13	Skin	SKIN	13	A/N	2,1	Yes

Visit/Timepoint Metadata Library. This library is populated based on visits and data collection timepoints described in the protocol. Visits and timepoints are selected based on what will be shown in the display.

Visit ID	Visit Name	Visit Number	Study Day	Window_Minimum	Window_Maximum	Select
1	Baseline	1	1			Yes
2	Baseline	1	1			Yes
3	Baseline	1	1			Yes
4	Day 7	2	7	5	9	Yes
5	Day 7	2	7	5	9	Yes
6	Day 7	2	7	5	9	Yes
7	Day 7	2	7	5	9	Yes
8	Day 7	2	7	5	9	Yes
9	Day 35	3	35	35	37	Yes
10	Unscheduled	77				No
11	Unscheduled	77				No
12	Unscheduled	77				No
13	Early Termination	88				No
14	End of Study	99				No

Variable Metadata Library. Certain displays require that some ADaM permissible variables be included in ADaM dataset(s). Displays within the display library are linked to a variable library of permissible and conditional ADaM variables. For example, the display selected is a shift table. This requires that BASE, BASEC, SHIFT, and SHIFTYN be included in the ADPE dataset.

Display ID	Display Type	Display Identifier	Display Title	ADaM Variables
61	Table	PE_TXA_01	Summary of Physical Examination Findings by Treatment Group and Visit	NA
62	Table	PE_TXB_01	Shift in Physical Examination Findings from Baseline to End of Study by Treatment Group	ABLFL, BASE, BASEC, SHIFTY, SHIFTYN
63	Table	PE_TXB_01	Shift in Physical Examination Findings from Baseline to End of Study by Treatment Group	ABLFL, BASE, BASEC, SHIFTY, SHIFTYN
64	Table	PE_TXB_02	Shift in Physical Examination Findings from Baseline to End of Study by Treatment Group	ABLFL, BASE, BASEC, SHIFTY, SHIFTYN

Treatment Metadata Library. This library is populated based on protocol-specified treatment groups—selections are made by display.

Treatment ID	Treatment Number	Treatment Code	Treatment Name	Treatment Period	Select
1	1	A	Active 5mg	Double Blind	Yes
2	2	B	Active 10mg	Double Blind	Yes
3	3	C	Active 20mg	Double Blind	Yes
4	4	D	Placebo	Double Blind	Yes
5	5	E	Screen Failure	Open Label	No
6	6	F	Screen Failure	Open Label	No