

Implementing ADaM Using SAS Clinical Standards Toolkit 1.4®



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Implementing ADaM 2.1 in Clinical Toolkit 1.4

- What is SAS Clinical Standards Toolkit?
- Process for Implementing ADaM
- Sample Study
- Validation Checks for ADaM
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- More Information

What is SAS Clinical Standards Toolkit?

- Focuses primarily on support of clinical research activities and initially focusing on standards as defined by CDISC, but not limited to CDISC.
- A collection of SAS based “tools” providing an initial set of standards and functionality that will evolve and grow with future updates and releases.
- Designed as an integral part of Clinical Data Integration (CDI), but is available to all SAS users as open source SAS macros, code , and data sets.
- Available free with the base SAS product.

What is SAS Clinical Standards Toolkit?

- Clinical Standards Toolkit 1.4 available with SAS 9.3

On the following platforms:

- Windows 32
 - Windows for x64
 - Linux for x64
 - Solaris SPARC
 - Solaris AMD
 - HP-UX Itanium
- Availability: Q4 2011

Process for Implementing ADaM

Three steps are required to register a standard

1. Create a folder structure in the Toolkit `cstGlobalLibrary` directory.
2. Create the required data sets needed by the Toolkit.
3. Register the standard to the Toolkit.

How do we know what is needed to proceed? The key is the `standards.sas7bdat` data set.

Process for Implementing ADaM

The standards data set is required and contains information about the standard provided by the user. Three columns determine the structure of the standard.

- Is this a data standard (Y/N)? [isdatastandard] - Set to Y – Requires reference_columns and reference_tables and initialize.properties.
- Standard supports validation (Y/N)? [supportsvalidation] - Set to Y. Requires validation_master and reference metadata above. Requires validation and report property files.
- Is this an xml-based standard (Y/N)? [isxmlstandard] - Set to N. When the ADaM define.xml is finalized this will be set to Y and implemented

Process for Implementing ADaM

Folder Structure

1. SAS Implemented standards will continue to use standardized Toolkit folder structure. Customized standards can use their own naming conventions
2. Data standard required /metadata, /programs, and / control folders.
3. Validation required /validation/control and /messages.
4. /macros folder for ADaM specific macros created by SAS
5. Must reside in the CST Global Root Directory

Process for Implementing ADaM

Required Files

- Data Standard:
 - Standards - metadata about the ADaM
 - Standardsasreferences – where things are
 - Reference_tables (Class_tables) – table metadata (ADSL, BDS, etc)
 - Reference_coumns (Class_columns) – column metadata
 - Initialize.properties – global macro settings
- Supports Validation:
 - Validation_master – the validation checks provided by the ADaM team
 - Messages – the descriptive text for each validation check
 - Validation.properties – global macro settings
 - Report.properties – global macro settings

Process for Implementing ADaM

Register ADaM to the Toolkit

/*Step 1.

Ensure that the macro variable pointing to the global standards library exists.*/

```
%cstutil_setcstgroot;
```

/*Step 2.

Register the standard with the Toolkit global standards library*/

```
%cst_registerStandard(  
    _cstRootPath=%nrstr(&_amp;cstGRoot./standards/cdisc-adam-2.1) ,  
    _cstControlSubPath=control ,  
    _cstStdDSName=standards ,  
    _cstStdSASRefsDSName=StandardSASReferences) ;
```

At this point, ADaM is registered to the Toolkit

Sample Study

Generated sample study based on SDTM 3.1.2 sample study.
The sample study consists of the following types of data:

- Clean analysis data sets to mimic an actual submission and used to generate the analysis reports. These include ADSL, ADAE, and ADQS
- “Dirty” data and metadata to test the validation process
- Hard to create ADAE based on BDS structure – used a draft of The ADaM Data Structure for Adverse Event Analysis Version 1.0.

Sample Study

Generated sample study based on SDTM 3.1.2 sample study.
The sample study consists of the following types of data:

- Mock tables
- Validation_control (study level validation_master)
- Report metadata
- Report output

Validation Checks for ADaM

The validation process for ADaM involved the following :

- Created validation_master from checks supplied by the ADaM Validation Checks V1.0 and V1.1 documents as provided by CDISC.
 - Currently have identified 159 unique checks.
- Messages data set
- Results and Metrics reporting provided
- Driver program to run the checks and reporting in base SAS
 - validate_data.sas
 - cst_report.sas
 - cst_metadatareport.sas

Validation Checks for ADaM

- Introduction of Cross Standard Validation - New to Toolkit and required development of two additional Toolkit validation macros.

cstcheck_crossstdcomparedomains.sas - compares inconsistencies in data values across standards.

Example: [ADaM] Sex= [SDTM] Sex=F

This macro requires use of `_cstCodeLogic` as a full DATA step or PROC SQL invocation.

Validation Checks for ADaM

- Introduction of Cross Standard Validation - New to Toolkit and required development of two additional Toolkit validation macros.

cstcheck_crossstdmetamismatch.sas - compares inconsistencies in metadata across standards.

Example: [ADaM] Sex=\$6 [SDTM] Sex=\$1

This macro requires use of `_cstCodeLogic` as a full DATA step or PROC SQL invocation

Validation Checks for ADaM

VIEWTABLE: TMP1.validation_master (Validation Checks, Master Superset)									
	Validation check identifier	Standard model	Source of check	Severity of check	Category of check	SAS macro module name	Domains/data sets to which check applies	Columns to which check applies	Code logic used within code
42	ADAM0044	CDISC-ADAM	CDISC	Error	ValueConsistency	cstcheck_columncompare	_ALL_	[**DTM][**TM-**DTM]	data work._cstProblems; set &_cstDSName.; if timepart(&_cstColumn1) ne &_cstColumn2; run;
43	ADAM0045	CDISC-ADAM	CDISC	Error	ValueConsistency	cstcheck_columncompare	_ALL_	[**DTM][**DT]	data work._cstProblems; set &_cstDSName.; if datepart(&_cstColumn1) ne &_cstColumn2; run;
44	ADAM0046	CDISC-ADAM	CDISC	Error	ValidValue	cstcheck_column	_ALL_-ADSL	**DY	if (&_cstColumn=0) then _cstError=1;
45	ADAM0047	CDISC-ADAM	CDISC	Error	Present/Populated	cstcheck_columnexists	ADSL	SITEID	
46	ADAM0048	CDISC-ADAM	CDISC	Error	Present/Populated	cstcheck_columnexists	ADSL	**FL	
47	ADAM0049	CDISC-ADAM	CDISC	Error	Present/Populated	cstcheck_columnexists	ADSL	AGE	
48	ADAM0050	CDISC-ADAM	CDISC	Error	Present/Populated	cstcheck_columnexists	ADSL	AGEU	
49	ADAM0051	CDISC-ADAM	CDISC	Error	Present/Populated	cstcheck_columnexists	ADSL	SEX	
50	ADAM0052	CDISC-ADAM	CDISC	Error	Present/Populated	cstcheck_columnexists	ADSL	RACE	
51	ADAM0053	CDISC-ADAM	CDISC	Error	ValueConsistency	cstcheck_crossstdcomparedomains	_ALL_	STUDYID+USUBJID	proc sql noprint;create table work._cstproblems as select &_cstSQLColList from &_cstDSName except select &_cstSQLColList from &_cstCrossDataLib..dm; quit;

Validation Checks for ADaM

Example of an ADaM Report

SAS Clinical Standards Toolkit 1.4 CDISC-ADAM 2.1 VALIDATION

Process Results, CheckID: ADAM0053

Description: Invalid STUDYID/USUBJID combination not found in the SDTM Demographics domain

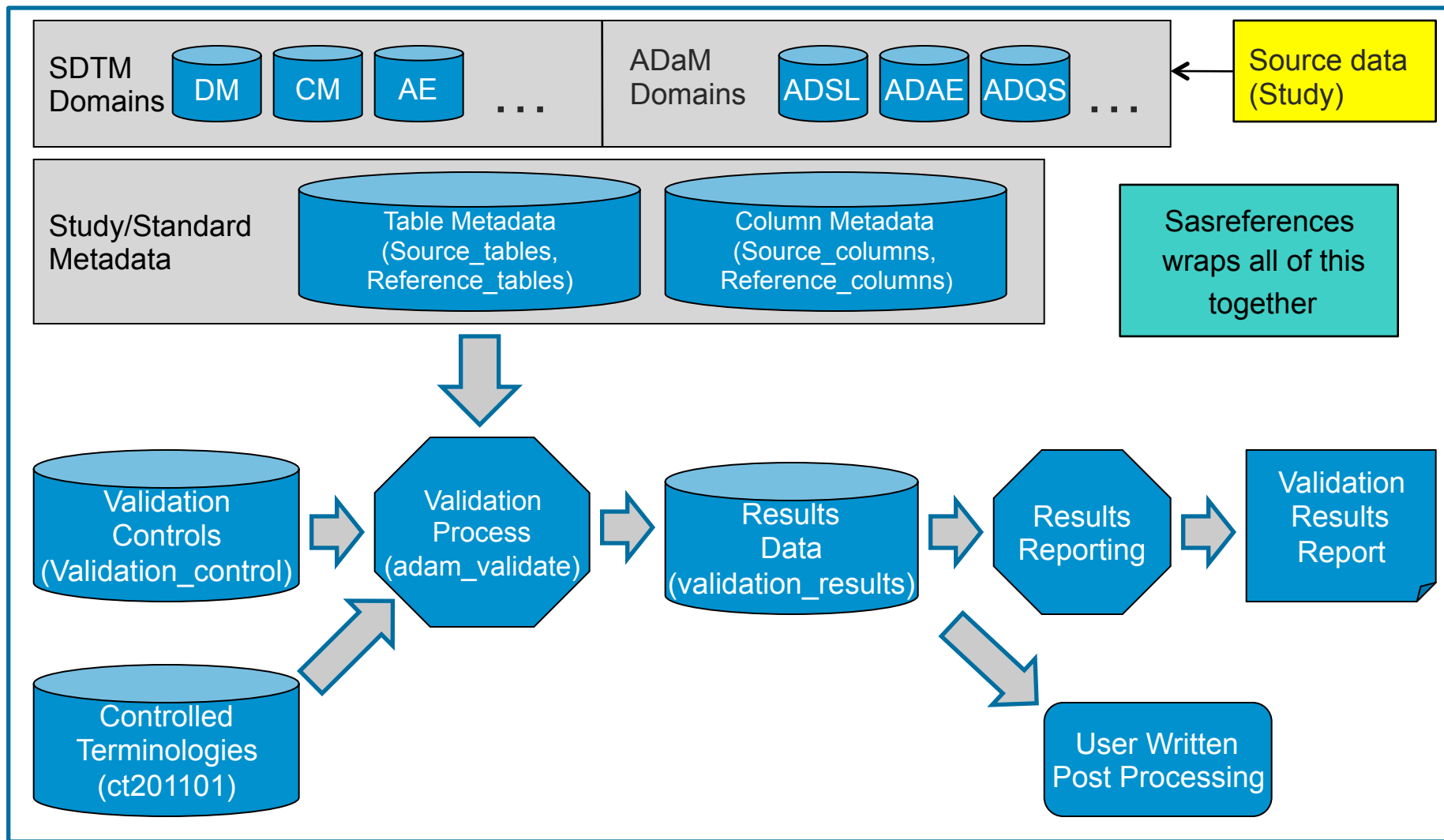
Check scope: (Tables) _ALL_, (Columns) STUDYID+USUBJID

Source: CDISC (53)

Validation check macro: cstcheck_crossstdcomparedomains, using source metadata

Check Invocation	Seq #	Source Data	Result Identifier	Message	Severity	Problem Detected?	Actual Value	Keys
1	1	SRCDATA.ADAE	ADAM0053	The values of USUBJID are not present in SDTM.DM	Error	Yes	STUDYID=SASCSTDDEMODATA, USUBJID=S999P999	USUBJID=S999P999,AETERM=., AESTDY=.
1	2	SRCDATA.ADQS	ADAM0053	The values of USUBJID are not present in SDTM.DM	Error	Yes	STUDYID=SASCSTDDEMODATA, USUBJID=S999P999	USUBJID=S999P999,PARAM=.
1	3	SRCDATA.ADSL	ADAM0053	The values of USUBJID are not present in SDTM.DM	Error	Yes	STUDYID=SASCSTDDEMODATA, USUBJID=S999P999	USUBJID=S999P999

Validation of the ADaM Standard



Report Processing Example

- The SAS Clinical Standards Toolkit representation of the ADaM standard includes a sample implementation of an analysis reporting methodology.
- The sample reporting methodology provided within the SAS Clinical Standards Toolkit is intended to be representative of similar industry methodologies.
- The intent is not to provide a definitive methodology, but to illustrate the interaction of reporting components through adoption of the ADaM standard.

Report Processing Example

Key Clinical Trial Reporting Components Addressed in Toolkit

Analysis Results (Tables, Listing, and Figures)	The set of statistical displays (for example, text, tabular or graphical presentation of results) or inferential statements such as p-values or estimates of treatment effect.
TLF Metadata (to include table shells)	Commonly provided as “table shells” which provide templates for the statistical displays. May also include display-specific metadata (often as Microsoft Excel files) used by the analysis programs to generate the displays.
Analysis Results Metadata	Defined by the Analysis Data Model Document, Section 5.3.
Analysis Programs	Programming code to use the analysis data sets (and optionally TLF metadata) to create the analysis results.

Watching the progress of the **Analysis Data Model (ADaM) Examples in Commonly Used Statistical Analysis Methods** document currently in draft form.

Report Processing Example

tlf_titles

Table 14.2.01
Summary of Demographic and Baseline Characteristics
Intent to Treat

		Placebo (N=xxx)	Low Dose (N=xxx)	High Dose (N=xxx)	Total (N = xxx)
		n (%)	n (%)	n (%)	n (%)
Age (Years)	n	xxx	xxx	xxx	xxx
	Mean	xx.x	xx.x	xx.x	xx.x
	STD	x.xx	x.xx	x.xx	x.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx.x	xx.x	xx.x	xx.x
	Max	xx.x	xx.x	xx.x	xx.x
Age	<30 years	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)
	– 45 years	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)
	≥ 5 years	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)
Sex	Female	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)
	Male	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)
Race	Asian	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)
	Black	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)
	Caucasian	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)
	Hispanic	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)
	Other	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)	xxx (yy.y%)

tlf_statistics

tlf_rows

tlf_footnotes

Produced by SAS Clinical Standards Toolkit at YYYY-MM-DDThh:mm:ss
<program name.1st>

Report Processing Example

Tlf_master data sets contains information about each defined table and “feeds” this information to the **analyze_data** driver program

	Unique identifier for analysis display	Display type (Table Listing Figure)	Page Orientation (Landscape Portrait)	Default display line size	Display Code Path	Display justification (L C R)
1	Table_14.2.01	Table	Landscape	132	&studyRootPath/analysis/code/Table_14.2.01.sas	C
2	Table_14.3.1.1	Table	Landscape	132	&studyRootPath/analysis/code/Table_14.3.1.1.sas	C

Analyze_data.sas – the driver code that uses the report metadata to generate the reports that are defined to it. This can be submitted in a base SAS session.

Report Processing Example

Table_14.2.01
Summary of Demographic and Baseline Characteristics
Intent to Treat

Example generated from running
analyze_data.sas Toolkit driver
program.

Table reproduced using metadata
defined for the process. Note the
footnotes as they appeared on the
mock table are absent.

They were not defined to the metadata.

		Placebo (N=21)	Low Dose (N=23)	High Dose (N=22)	Total (N=66)
		n(%)	n(%)	n(%)	n(%)
Age (Years)	n	21	23	22	66
	Mean	34.9	38.6	37.6	37.1
	STD	10.84	8.52	10.88	10.07
	Median	33	40	37	38
	Min	20	21	18	18
	Max	53	48	54	54
Age	<30 years	8 (38.1%)	5 (21.7%)	5 (22.7%)	18 (27.3%)
	30-45 years	7 (33.3%)	11 (47.8%)	10 (45.5%)	28 (42.4%)
	>45 years	6 (28.6%)	7 (30.4%)	7 (31.8%)	20 (30.3%)
Sex	Female	15 (71.4%)	11 (47.8%)	12 (54.5%)	38 (57.6%)
	Male	6 (28.6%)	12 (52.2%)	10 (45.5%)	28 (42.4%)
Race	Asian	4 (19.0%)	4 (17.4%)	1 (4.5%)	9 (13.6%)
	Black	2 (9.5%)	6 (26.1%)	4 (18.2%)	12 (18.2%)
	Caucasian	9 (42.9%)	9 (39.1%)	11 (50.0%)	29 (43.9%)
	Hispanic	2 (9.5%)	4 (17.4%)	5 (22.7%)	11 (16.7%)
	Other	4 (19.0%)		1 (4.5%)	5 (7.6%)

ADaM Information

- CDISC Analysis Data Model, Version 2.1 available at www.cdisc.org/adam
- CDISC ADaM Implementation Guide, Version 1.0 available at www.cdisc.org/adam
- CDISC ADaM Basic Data Structure for Time-to-Event Analysis 1.0 at www.cdisc.org/adam
- The ADaM Data Structure for Adverse Event Analysis Version 1.0 Prepared by the CDISC Analysis Data Model Team (ADaM)
- Analysis Data Model (ADaM) Examples in Commonly Used Statistical Analysis Methods Document for Public Review at www.cdisc.org.adam

Clinical Standards Toolkit Resources

- SAS Clinical Standards Toolkit V1.4 User's Guide will be posted at:

<http://support.sas.com/documentation/onlinedoc/clinical/index.html>

- SAS Knowledge Base/Focus Area

<http://support.sas.com/rnd/base/cdisc/cst/index.html>

- Availability of updates will generally be posted to the SAS and Clinical Trials Community, available at:

http://communities.sas.com/community/sas_and_clinical_trials

Questions?



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