Implementing ADaM Using SAS Clinical Standards Toolkit 1.4®
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
- Report Processing Example
- 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

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.

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(&_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_crossstdcomparereadomains.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
## ViewTable: TMP1.validation_master (Validation Checks, Master Superset)

<table>
<thead>
<tr>
<th>Validation check identifier</th>
<th>Standard model</th>
<th>Source of check</th>
<th>Severity of check</th>
<th>Category of check</th>
<th>SAS macro module name</th>
<th>Domains/data sets to which check applies</th>
<th>Columns to which check applies</th>
<th>Code logic used within code</th>
</tr>
</thead>
<tbody>
<tr>
<td>42  ADAM0044     CDISC-ADAM CDISC        Error       ValueConsistency      cstcheck_columncompare               <em>ALL</em>  [“DTM”] [“TM”] [“DTM”]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>43  ADAM0045     CDISC-ADAM CDISC        Error       ValueConsistency      cstcheck_columncompare               <em>ALL</em>  [“DTM”] [“TM”] [“DTM”]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>44  ADAM0046     CDISC-ADAM CDISC        Error       ValueConsistency      cstcheck_column               <em>ALL</em>  ADSL  [“DY”]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45  ADAM0047     CDISC-ADAM CDISC        Error       ValueConsistency      cstcheck_column               <em>ALL</em>  ADSL  SITEID</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>46  ADAM0048     CDISC-ADAM CDISC        Error       ValueConsistency      cstcheck_column               <em>ALL</em>  ADSL  [“FL”]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>47  ADAM0049     CDISC-ADAM CDISC        Error       ValueConsistency      cstcheck_column               <em>ALL</em>  ADSL  AGE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48  ADAM0050     CDISC-ADAM CDISC        Error       ValueConsistency      cstcheck_column               <em>ALL</em>  ADSL  AGEU</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>49  ADAM0051     CDISC-ADAM CDISC        Error       ValueConsistency      cstcheck_column               <em>ALL</em>  ADSL  SEX</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50  ADAM0052     CDISC-ADAM CDISC        Error       ValueConsistency      cstcheck_column               <em>ALL</em>  ADSL  RACE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>51  ADAM0053     CDISC-ADAM CDISC        Error       ValueConsistency      cstcheck_crossstdcomparedomains               <em>ALL</em>  STUDYID+USUBJID</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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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: cstarcheck_crossstddomains, using source metadata

<table>
<thead>
<tr>
<th>Check Invocation</th>
<th>Seq #</th>
<th>Source Data</th>
<th>Result Identifier</th>
<th>Message</th>
<th>Severity</th>
<th>Problem Detected?</th>
<th>Actual Value</th>
<th>Keys</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>SRCDATA.ADAE</td>
<td>ADAM0053</td>
<td>The values of USUBJID are not present in SDTM.DM</td>
<td>Error</td>
<td>Yes</td>
<td>STUDYID=SASCSTDEMODATA, USUBJID=S999P999, AETERM=, AESTDY=</td>
<td>USUBJID=S999P999</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>SRCDATA.ADQS</td>
<td>ADAM0053</td>
<td>The values of USUBJID are not present in SDTM.DM</td>
<td>Error</td>
<td>Yes</td>
<td>STUDYID=SASCSTDEMODATA, USUBJID=S999P999</td>
<td>USUBJID=S999P999, PARAM=</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>SRCDATA.ADSL</td>
<td>ADAM0053</td>
<td>The values of USUBJID are not present in SDTM.DM</td>
<td>Error</td>
<td>Yes</td>
<td>STUDYID=SASCSTDEMODATA, USUBJID=S999P999</td>
<td>USUBJID=S999P999</td>
</tr>
</tbody>
</table>
Validation of the ADaM Standard

Study/Standard Metadata

- Table Metadata (Source_tables, Reference_tables)
- Column Metadata (Source_columns, Reference_columns)

Validation Process (adam_validate)

Results Data (validation_results)

Validation Results Report

User Written Post Processing

Sasreferences wraps all of this together

Source data (Study)

SDTM Domains
- DM
- CM
- AE

ADaM Domains
- ADSL
- ADAE
- ADQS

Controlled Terminologies (ct201101)

Validation Controls (Validation_control)
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.
### Key Clinical Trial Reporting Components Addressed in Toolkit

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysis Results (Tables, Listing, and Figures)</td>
<td>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.</td>
</tr>
<tr>
<td>TLF Metadata (to include table shells)</td>
<td>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.</td>
</tr>
<tr>
<td>Analysis Results Metadata</td>
<td>Defined by the Analysis Data Model Document, Section 5.3.</td>
</tr>
<tr>
<td>Analysis Programs</td>
<td>Programming code to use the analysis data sets (and optionally TLF metadata) to create the analysis results.</td>
</tr>
</tbody>
</table>

Watching the progress of the **Analysis Data Model (ADaM) Examples in Commonly Used Statistical Analysis Methods** document currently in draft form.
## Table 14.2.01
Summary of Demographic and Baseline Characteristics Intent to Treat

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=xxx)</th>
<th>Low Dose (N=xxx)</th>
<th>High Dose (N=xxx)</th>
<th>Total (N = xxx)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (Years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>xxx</td>
<td>xxx</td>
<td>xxx</td>
<td>xxx</td>
</tr>
<tr>
<td>Mean</td>
<td>xx.x</td>
<td>xx.x</td>
<td>xx.x</td>
<td>xx.x</td>
</tr>
<tr>
<td>STD</td>
<td>x.x</td>
<td>x.x</td>
<td>x.x</td>
<td>x.x</td>
</tr>
<tr>
<td>Median</td>
<td>xx.x</td>
<td>xx.x</td>
<td>xx.x</td>
<td>xx.x</td>
</tr>
<tr>
<td>Min</td>
<td>xx.x</td>
<td>xx.x</td>
<td>xx.x</td>
<td>xx.x</td>
</tr>
<tr>
<td>Max</td>
<td>xx.x</td>
<td>xx.x</td>
<td>xx.x</td>
<td>xx.x</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 years</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
</tr>
<tr>
<td>30-45 years</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
</tr>
<tr>
<td>&gt;45 years</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
</tr>
<tr>
<td>Male</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
</tr>
<tr>
<td>Black</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
</tr>
<tr>
<td>Other</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
<td>xxx (yy.y%)</td>
</tr>
</tbody>
</table>

Produced by SAS Clinical Standards Toolkit at YYYY-MM-DD/Thh mm ss <program name sas>
Report Processing Example

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

<table>
<thead>
<tr>
<th>Unique identifier for analysis display</th>
<th>Display type (Table</th>
<th>Listing</th>
<th>Figure)</th>
<th>Page Orientation (Landscape</th>
<th>Portrait)</th>
<th>Default display line size</th>
<th>Display Code Path</th>
<th>Display justification (L</th>
<th>C</th>
<th>R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Table_14.2.01</td>
<td>Table</td>
<td>Landscape</td>
<td></td>
<td></td>
<td>132</td>
<td>&amp;studyRootPath/analysis/code/Table_14.2.01.sas</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Table_14.3.1.1</td>
<td>Table</td>
<td>Landscape</td>
<td></td>
<td></td>
<td>132</td>
<td>&amp;studyRootPath/analysis/code/Table_14.3.1.1.sas</td>
<td>C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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.
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)
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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